The impact of an enzyme-modified enriched maize-based supplement on the anthropometric nutritional status of institutionalised HIV^{+} children

Erika van der Walt

Dissertation submitted as fulfillment of the requirements for the degree
M Nutrition

in the
Faculty of Health Sciences
Department of Nutrition and Dietetics
University of the Free State
Bloemfontein
South Africa
July 2013

Study leader
Prof A Dannhauser

Co-study leader
Prof FJ Veldman

DECLARATION

I certify that the dissertation hereby submitted by me for the M Nutrition qualification at the University of the Free State is my independent effort and had not previously been submitted for a qualification at another university/faculty. I furthermore waive copyright of the dissertation in favour of the University of the Free State.

Erika van der Walt

July 2013

ACKNOWLEDGEMENTS

This study would not have been possible without:

My Heavenly Father, for giving me the strength and ability to complete this study;

My study leader, Prof. A Dannhauser (Department of Human Nutrition, University of the Free State) for her patience, guidance and support throughout this project;

My co-study leader, Prof. FJ Veldman (Dietetics and Human Nutrition, School of Agricultural, Earth and Environmental Sciences, College of Agriculture, Engineering and Science, University Kwazulu Natal) for his valuable inputs;

Prof. G Joubert, (Department of Biostatistics, University of the Free State) for the statistical analysis of the data;

Diva Nutritional Products for supplying both the experimental and control supplements for the project;

My co-researchers, Mrs. L Steenkamp and Ms. C Cox for their assistance and inputs during the study;

The study participants and the management and personnel of the care centres;

My husband Hendrik, sons Herman and Bernard, friends, and my business partner Marnelle for their patience, support and encouragement. A special thank you to my daughter Elzette and her friend Jarina, for walking the extra mile with me.

TABLE OF CONTENTS **PAGE**

CHAPTER 3 – METHODOLOGY

LIST OF TABLES

LIST OF FIGURES

LIST OF APPENDICES

LIST OF ABBREVIATIONS

ADA	American Dietetics Association
AIDS	acquired immune deficiency syndrome
ARV	antiretroviral drugs
ART	antiretroviral treatment
BMI	body mass index
BMI/A	body mass index-for-age
BMIZ	body mass index Z-score
CDC	Centres for Disease Control
CMV	cytomegalovirus
CNS	central nervous system
DNA	deoxyribonucleic acid
ELISA	enzyme-linked immunosorbent assays
FANTA	Food and Nutrition Technical Assistance
FAO	Food and Agricultrural Organisation
FFM	fat free mass
GI	gastro-intestinal
H/A	height-for-age
HAZ	height-for-age Z-score
HC	head circumference
HC/A	head circumference-for-age
HIV	human immunodeficiency virus
HVC	hepatitis-C infection

INP	Integrated Nutrition Program
IMCI	Integrated Management of Childhood Illness
KS	Kaposi's sarcoma
LMS	lambda, mu, and sigma estimation procedure
MDR	multi drug resistant (tuberculosis)
MGRS	Multicentre Growth Reference Study
MRC	Medical Research Council
MTCT	mother-to-child transmission
MUAC	mid upper arm circumference
MUAC/A	mid upper arm circumference-for-age
NAIDS	nutritionally acquired immune deficiency
NCHS	National Centre for Health Statistics
NFCS	national food consumption survey
NFCS-FB	national food consumption survey fortification base
NHANES	National Health and Nutrition Examination Survey
nm	nanometer
PCP	*pneumocystis carinii* pneumonia
PEM	protein-energy malnutrition
RNA	ribonucleic acid
RT	reverse transcriptase
RUTF	ready-to-use therapeutic food
RDA	Recommended Dietary Allowance
RSA	Republic of South Africa
SAVACG	South African Vitamin A Consultative Group

SD	standard deviation
TB	tuberculosis
TSF	triceps skinfold thickness
TSF/A	triceps skinfold thickness-for-age
TUA	total upper arm area
UAFA	upper arm fat area
UAFA/A	upper arm fat area-for-age
UAMA	upper arm muscle area
UAMA/A	upper arm muscle area-for-age
UN	United Nations
UNAIDS	Joint United Nations Programme on HIV/AIDS
UNICEF	United Nations Children's Fund
W/A	weight-for-age
WAZ	weight-for-age Z-score
WHA	World Health Assembly
WHO	World Health Organisation
WITS	Women and Infants Transmission Study

CHAPTER 1 – INTRODUCTION

The human immune deficiency virus (HIV), the infective agent of acquired immune deficiency syndrome (AIDS), negatively influences the health, quality of life and nutritional status of infected individuals. The nutritional status of HIV-positive (HIV^+) children is even more at risk than that of HIV^+ adults (the term HIV-infected will replace HIV^+ throughout the rest of this document, and HIV/AIDS will refer to the illness or condition caused by HIV). Balanced nutrition that provides in the specific needs of the HIV-infected person is one of the most important goals of the successful management of HIV/AIDS, in all age groups. Yet, in a developing country such as South Africa, especially for the poor, it is not always easy to follow nutrition guidelines. The use of food supplements offers an easy and convenient way of improving nutritional intake, especially where supplementation is provided by government. However, with the overwhelming number of food and food-based nutritional supplements on the market, each with its own claim to unique benefits, scientific evaluation of products should guide both consumers and government in selecting the most effective products.

1.1 BACKGROUND

HIV/AIDS was first recognised in 1981 when young homosexual men in the United States presented with symptoms that at that stage were thought to be cancer or even the result of drug abuse. By 1983 HIV had been identified as the etiological agent (UNAIDS & WHO, 2003a:3). The infection was initially considered to be restricted to gay men, but it was soon discovered that the infection could also be transmitted to heterosexual men, women and also children through blood and other body fluids (Karim *et al.*, 2009:922).

A number of strains of HIV have been identified. The prognosis of those infected also depends on the strain. HIV-1 is the strain that causes HIV/AIDS, and several subtypes were identified. Epidemiological studies show how the subtypes of the virus are geographically distributed, with subtype B more predominant in the United States of America, and non-B subtypes particularly prevalent in Africa and Asia. Subtype C is most commonly transmitted in the heterosexual population of South Africa (Karim *et al.*, 2009:922).

By the mid-1980's it became clear that the virus had spread in epidemic proportions throughout most of the world (UNAIDS & WHO, 2003a:3), and soon the epidemic reached pandemic proportions. In South Africa, the epidemic reached pandemic status around 1995/6 (Govender:Online).

Certain geographic areas and countries, however, carry larger shares of the burden than others. Globally, in 2009 an estimated 33.3 million people were infected with HIV (UNAIDS, 2010a:180). Sub-Saharan Africa carries the largest share, namely 68%, or 22.5 million people (UNAIDS, 2010b:25) infected with HIV. In South Africa alone an estimated 5.6 million people were living with HIV in 2009. This puts South Africa first as the country with the highest HIV/AIDS incidence in the world (UNAIDS, 2010b:28; UNAIDS & WHO, 2003a:6).

Over a period of 30 years after the first diagnosis of HIV/AIDS in the United States, the number of children infected with HIV worldwide has increased dramatically, especially in developing countries (Rivera, 2012:Online). In 2009 an estimated 2.5 million of the global HIV-infected population were children under the age of 15 years (UNAIDS, 2010a:180). In the same year in South Africa an estimated 330 000 children aged 14 years and younger were living with HIV/AIDS (UNAIDS, 2010a:182). During 2010 an estimated 40 000 children in South Africa were newly infected with HIV (Statistics SA, 2010:8).

This earlier sharp increase of HIV infection amongst children can be attributed mainly to the rise in numbers of HIV-infected women of childbearing age, where an HIV-infected mother transmits the virus to her baby or young child. Transmission of the virus from the mother to the child, or mother-to-child transmission of HIV (MTCT), has received widespread attention from researchers and health authorities alike. MTCT can occur during pregnancy, during childbirth or through breastfeeding (Rivera, 2012:Online).

HIV/AIDS has dramatically influenced life expectancy and mortality rates. Since 1998, HIV/AIDS has claimed at least 1 million lives annually in sub-Saharan Africa. The death toll peaked in 2005 with 1.7 million HIV/AIDS deaths. In 2005 HIV/AIDS was rated the fourth-leading cause of death worldwide (WHO, 2005:81). After 2005, however, as anti-retroviral therapy (ART) became more widely available, the number of people dying from HIV/AIDS

and HIV/AIDS-related causes has steadily declined. In 2010 HIV/AIDS related deaths were 29% fewer than in 2005 (WHO/UNAIDS/UNICEF, 2011:25).

Until 2007, South Africa's mortality rates did not reflect HIV/AIDS as a cause of death, but the deaths due to the HIV/AIDS epidemic can be assumed to be reflected in the overall rise in mortality rates. In South Africa, the number of annual deaths due to all causes has risen sharply from 316 559 deaths in 1997 to 607 184 deaths in 2006 (Statistics SA, 2008:10,11,43). The percentage HIV/AIDS deaths for all sex and age groups in South Africa was 35.8% in 2009 (211 903 persons), 34.6% in 2010 (201 174 persons), 34.6% in 2011 (200 259 persons), 33.5% in 2012 (191 620 persons) and 31.9% (178 373 persons) in 2013 (Statistics SA, 2013:7).

The increase in life expectancy of people living with HIV, and the subsequent decline or levelling out of HIV/AIDS deaths is, unfortunately, not yet the end of the problems caused by the pandemic. As the use of ART continues to expand, the number of people surviving with HIV will continue to rise (WHO/UNAIDS/UNICEF, 2011:19). Still, it is expected that HIV/AIDS deaths will continue to dwarf other causes of mortality for at least another 10 years (from 2009), even if as much as 90% ART coverage is achieved (Harrison, 2010:Online).

Households affected by HIV/AIDS will suffer under long-term negative effects for many more years. The negative effects caused by HIV/AIDS on affected households are also carried through to the children of the household, whether they are infected with HIV or not. Typical problems of HIV/AIDS-affected households are that one or both parents may be chronically ill (UNICEF, 2006:25), and not able to work, leading to a loss of income (Collins & Leibbrandt, 2007:S79) and subsequent food insecurity (UNICEF, 2006:26; World Bank, 2007:40). Often the child has to stay out of school to earn money or to care for the sick parent, carry the responsibility of the household, purchase and prepare food, etc. In the process the child is deprived of a school education and the privilege of being a child (UNICEF, 2006:24).

In a household affected by HIV/AIDS, it is inevitable that the child will eventually lose one or both parents to the disease. An estimated 40% of children with HIV-infected parents may

lose one of their parents to the disease before reaching adolescence, and 25% will lose a parent before they reach the age of five years (UNICEF, 2006:26). The loss of a parent has an immense emotional impact on a child, over and above the negative financial impact due to the funeral costs and the loss of an income in cases where the diseased parent still had an income (Collins & Leibbrandt, 2007:S79), which negatively impacts on household food security.

In sub-Saharan Africa, an estimated 11.6 million children had been orphaned by HIV/AIDS as of 2007 (WHO, 2009a:3). An orphan is defined as a child younger than 17 years who has lost one or both parents (UNICEF, 2006:5). UNAIDS (2010a:186) estimated that South Africa had 1.9 million HIV/AIDS orphans in 2009. In 2010, Statistics SA (2010:8) estimated the number of HIV/AIDS orphans in South Africa at 1.99 million.

Very often relatives, often older relatives, have to become the orphan's primary carers; the orphans may have to relocate from their familiar neighbourhood; siblings may even be separated, all of which can harm their development. This places an additional financial burden on relatives who often cannot carry the burden, putting the child at risk for malnutrition, poor health and, if the child is HIV-infected, faster progression to AIDS. Child-headed households are often the other alternative, leading to children having to leave school to take responsibility for the care of an ill parent and often to take care of younger siblings as well, over and above having to run the household with little or no resources (UNICEF, 2006:3-9).

It is expected that the number of HIV/AIDS orphans will continue to grow or remain high for years (UNICEF, 2006:9). This emphasises the importance of ensuring that government policies on HIV/AIDS also include ways of ensuring that orphans, including HIV/AIDS orphans, are well cared for (Case *et al.*, 2004:483-507; UNICEF, 2006:26-31).

Many HIV/AIDS orphans end up in care centres, often because of the inability of relatives to take them in (UNICEF, 2006:23). Some of these centres are now specifically caring for children infected or affected by HIV/AIDS. Major problems faced by these centres are the lack of specific recommendations or guidelines for nutrition support for these children, as

well as a lack of finances and skilled staff to provide optimal nutrition to the children (UNICEF, 2006:24). Nutrition intervention through the use of food supplements in these care centres can offer a relatively easy way to improve the nutritional value of the available diet. The correct choice of food supplement is however very important, keeping in mind that it should fit a tight budget and be easy to use.

HIV-infected children are more vulnerable to malnutrition than children not infected (Kimani-Murage *et al.*, 2011:1,11). Nutritional status is also an important predictor of survival in HIV-infected children (Fergusson *et al.*, 2009:512; Preidis, 2011:488, 2009:35). HIV infection negatively influences nutritional status through various mechanisms, including increased energy and nutrient needs and decreased food intake (Benjamin *et al.*, 2003:2332; WHO, 2003a:4). Due to the increased nutritional needs to ensure normal growth and development, the nutritional status of HIV-infected children is even more at risk than in HIV-infected adults (WHO, 2003a:3-4; Bunn *et al.,* 2009:108, European Collaborative Study, 2003:e52-e59; Villamor *et al.*, 2005:65-67; Ramalho *et al.*, 2011:454). Poor nutritional status negatively influences health and immunity, putting the child at greater risk for infections and disease. This leads to a vicious cycle of impaired nutritional status and poor health, associated with a decrease in quality of life and even untimely death.

The importance of nutrition intervention to ensure better quality of life and a longer life expectancy in HIV-infected patients has been highlighted since the early days of the HIV pandemic. Nutrition intervention for HIV-infected children usually includes supplementation of the diet with energy-rich foods and macro- and micronutrients in quantities large enough to ensure that the child's needs for normal growth, as well as the additional needs caused by the infection, are reached (Arpadi *et al*., 2000:2500; ADA, 2000:713; Bobat *et al.*, 2001:203; Steenkamp *et al.*, 2009:135).

In 2005 the Consultation on Nutrition and HIV/AIDS in Africa put out a statement which called for the integration of nutrition into an essential package of care, treatment and support for people living with HIV/AIDS (WHO, 2005:1). When planned and implemented properly, the provision of food in addition to health care can have many benefits, e.g. by supporting treatment outcomes, improve targeting, helping with dissemination of

information and providing therapeutic effects on health and nutritional status (World Bank, 2007:39).

The World Bank has, in collaboration with national and international bodies such as the World Health Organization (WHO), United Nations Children's Fund (UNICEF), Food and Agriculture Organization of the United States (FAO), Food and Nutrition Technical Assistance Project (FANTA), compiled a document with guidelines and recommendations for the implementation of food support programs in the context of HIV/AIDS in areas struck by poverty and food insecurity (World Bank, 2007:3-5).

The South African government also engaged in efforts to provide nutritional support to individuals infected with and households affected by HIV/AIDS. The Integrated Nutrition Program (INP) was initiated in 1995 by the South African Department of Health. The INP included direct as well as indirect nutrition interventions to address the underlying causes of malnutrition. The provision of nutritional support to HIV-infected patients through all primary health care clinics forms part of the strategies of the INP (Department of Health, 2008:2-4). However, although the program forms part of a national strategy, it has to function within the restrictions of provincial government health budgets. Provincial governments need a product that will provide in all the nutritional needs of the target group, is palatable, culturally acceptable and affordable amidst an ever increasing number of patients in need of nutritional support. In order to provide the best possible options within these budget restrictions, the provincial governments need to revise and continuously seek for a product that will fulfil the nutritional needs of the HIV/AIDS patients, and an ever increasing need for food assistance.

1.2 PROBLEM STATEMENT

In South Africa malnutrition has been and still is a public health problem that requires priority. Malnutrition refers to both over- and undernutrition (Robinson et al., 1986:4). In South Africa, malnutrition is present both as overnutrition and obesity as well as undernutrition (Bradshaw *et al*. 2006:9). However, in the context of HIV, malnutrition refers to undernutrition, which is the focus of this research.

Malnutrition increases the risk of mortality in children infected with HIV (Villamor *et al*., 2005:65). On the hand of available information, the WHO recommends that nutrition forms a fundamental part of comprehensive packages of care for people living with HIV/AIDS. The prevention of malnutrition, or alternatively early intervention treatment with appropriate and adequate nutrition, can contribute to improved survival and quality of life of people living with HIV (WHO, 2003a:3,4,6).

In children living with HIV, the nutritional needs are increased due to the infection. It is essential that their diet provides in the needs for continued growth and development and also cover the higher needs resulting from the HIV infection to prevent undernutrition (WHO, 2003a:3,4,6; Oguntibeju *et al*., 2007:4327).

Findings from studies and from health care statistics have indicated that the prevalence of child malnutrition in South Africa has increased between 1999 and 2007. Since child malnutrition is an indicator of child health, the deterioration in child nutritional status is accompanied by a deterioration in child health. Underweight and stunting are the most common nutritional disorders in South Africa. In the recent past, two national comprehensive nutrition surveys were carried out in South Africa - the National Food Consumption Survey in 1999 and the National Food Consumption Survey Fortification Baseline in 2005, respectively. The results from these studies show that the national prevalence of stunting has decreased from 21.6% to 18%. The prevalence of underweight has remained statistically unchanged at 9.3%. However, when broken up in rural and urban areas, the prevalence of stunting and underweight in rural areas has reduced at the same time that it has increased in urban areas. The prevalence of wasting has also remained statistically unchanged on a national level, but when comparing rural and urban, the prevalence of wasting has decreased in the rural areas but has more than doubled in urban areas (NFCS, 2000:193; NFCS-FB, 2007:144). The highest HIV prevalence is also reported for the urban areas of South Africa. Therefore, on the hand of the vicious cycle of malnutrition and disease (Semba & Tang, 1999:182), it can be speculated that the poorer nutritional status of children in the urban areas can be a result of the higher prevalence of HIV in these areas.

In the Free State Province specifically the prevalence of moderate stunting in the age group one to nine years old is reported to be 28.2%, and 7.0% for severe stunting. With regard to underweight the prevalence in the same age group is reported to be 14.1% for moderate underweight and 2.2% for severe underweight (wasting). These figures highlight the fact that the Free State Province specifically needs to give special attention to child undernutrition as a priority (NFCS, 2000:193; NFCS-FB, 2007:144).

The majority of people in developing countries, including South Africa, depend on staple foods such as wheat, maize or rice for survival. Although the staple food is an inexpensive source of energy, it is a poor source of micronutrients. The South African Government has implemented the fortification of staple foods (maize meal, bread flour and bread) in order to increase the intake of specific micronutrients with the staple foods. However, although the fortified product helps to increase the intake of micronutrients, these foods do not have a high energy density unless the viscosity of the cooked product is high. Young children in general, cannot consume enough of the high viscosity food to meet their energy needs.

The addition of an enzyme, α-amylase, to starch-based foods such as maize porridge, reduces the viscosity while retaining energy density. It is hypothesised that the reduced viscosity will enable young children to consume more of the porridge, and thereby improve the propability that they would meet their energy and nutrient needs. A number of researchers have documented an increase in energy intake and improved growth in children consuming starch based diets with added α-amylase (Den Besten *et al.*, 1998:4, Gopaldas & Chinnamma, 1992:278; Chinnamma & Gopaldas, 1993:18).

A vitamin- and mineral enriched, maize-based supplement with added amylase has been used extensively by the Department of Health in their clinic based nutrition supplementation program for underweight children, including HIV-infected children. However, a need was identified to determine whether the added amylase holds any benefits specifically for HIV-infected children. The reported study was undertaken with the view to evaluate the impact of nutrition intervention with a vitamin- and mineral enriched maize-based supplement with added amylase on the anthropometric nutritional status of HIV-infected children.

1.3 AIM AND OBJECTIVES

This study formed part of a bigger study in which four researchers participated. The aim of this component of the study was to determine the impact of an enzyme-modified, enriched maize-based supplement on the anthropometric nutritional status of children infected with HIV living in semi-government / partly government funded institutions for HIV-infected and affected children in the Mangaung area of Bloemfontein.

The Objectives of the study were to:

- determine the anthropometric nutritional status of children in an experimental and a control group in available institutions before as well as after 16 weeks of nutrition supplementation with either an experimental or a control product.
- use the data obtained to evaluate and compare the impact of the experimental and control products on the anthropometric nutritional status of the children

1.4 STRUCTURE OF THE DISSERTATION

Chapter 1 provides an introduction with a short summary of the study structure and the role of this researcher, as well as background information to explain the need for the study, the aim and objectives of this study, as well as an outline of the structure of this dissertation. Chapter 2 contains a literature review in support of the study. The methodology and study design are described in Chapter 3, as well as the measurements taken, measuring techniques, validity and reliability, population and sampling, study procedures and statistical analysis. Chapter 4 describes the baseline data and data collected at the end of the study of the HIV-infected children in the care centres in Mangaung that were included in the study. Chapter 5 contains a discussion of the results, as well as conclusions and recommendations. Chapter 6 contains conclusions and recommendations based on the findings in the study. Summaries in English and Afrikaans are included at the back of the dissertation.

CHAPTER 2 - LITERATURE REVIEW

2.1 INTRODUCTION

Children comprises one of the largest groups infected and affected by HIV/AIDS. The scale of the epidemic in the adult population has unfortunately overshadowed the needs of HIV-infected children for a long time (UNICEF, 2010:Online). Progression of the disease and survival of children infected with HIV are not the same as in adults, and are influenced by a number of factors. HIV infection in children leads to a dramatic reduced life expectancy and poor quality of life.

Malnutrition, specifically undernutrition, and poor growth are important negative consequences of HIV infection in children. The main contributors to malnutrition in HIV-infected children are inadequate food and nutrient intake due to several dietary related factors Bobat *et al*., 2001:203; Dong & Imai, 2012:1006-1020, Fenton & Silverman, 2008:991-1-20). A large number of socio-economic factors also influence food and nutrient intake and consequently impact nutritional status. Malnutrition (undernutrition) can be classified through the use of anthropometric indices. Anthropometric nutritional status is evaluated and measured through the use of anthropometric measurements of, amongst others, height, weight, mid upper arm circumference and skinfold thickness. These measurements can be compared to reference data and standards to evaluate the anthropometric nutritional status of a selected population.

Strategies to manage the HIV epidemic have been redirected over the past few years and children infected and affected by HIV are now central to most strategies and actions to avert and address the consequences and further spread of the epidemic. Due to the important role of good nutrition to slow down the progression of the disease, all intervention strategies should target nutrition, usually through nutrition supplementation. Specific nutritional problems caused by HIV infection complicate nutrition intervention, and therefore care should be taken to ensure that nutrition supplements used for HIV-infected patients will provide maximum benefit even in the presence of existing nutritional deficiencies or problems that relate to the intake of food (Egge & Strasser, 2005:306).

This chapter provides some background in terms of HIV/AIDS, clinical manifestations of HIV infection, the relationship between malnutrition and HIV/AIDS, causes of malnutrition in HIV-infected children, indicators of anthropometric nutritional status and growth, and management of HIV in children.

2.2 HIV/AIDS

Information and knowledge regarding HIV/AIDS etiology and transmission, virology and immune response give a better understanding of the stages of HIV infection, HIV/AIDS progression in children and the influence of HIV/AIDS on infant and child mortality rates.

2.2.1 Etiology and transmission

HIV/AIDS is caused by the human immunodeficiency virus, a retrovirus, known as HIV. HIV is a complex member of the *Lentivirus* genus of the *Retroviridae* family (Weiss, 1993:1273-8). Different strains of the virus can be identified. HIV-1 is the most common strain as well as the most common cause of HIV infection in the Americas, Europe, Asia, and Sub-Saharan Africa. HIV-2 seems to have originated from West Africa and is also more common in that area (Reeves & Doms, 2002:1253), but is also found to a lesser degree in European countries. HIV-2 is less transmissible than HIV-1 and HIV-2 disease progresses more slowly than HIV-1 disease (Gilbert *et al*., 2003: 573).

Persons who are infected with HIV carry the virus in their blood and other body fluids, e.g. semen, saliva and breast milk (CDC, 2010:Online). Direct contact with the body fluids of the HIV-infected person provides a route for transmission of the virus. The integrity of the exposed site, the type and volume of the body fluid as well as the viral load determines the risk of infection. In adults and adolescents the major mode of transmission of HIV is sexually Rivera, 2012:Online). Transmission can also take place parenteral via contaminated blood products or via intravenous (IV) drug abuse. Adolescents commonly become infected by engaging in high-risk behaviours, which includes unprotected sexual intercourse, male homosexual intercourse and the use of injecting drugs (Cunningham *et al*., 2010:524).

In infants and young children, MTCT is a major route of infection (WHO, 2010b:6). MTCT can occur in utero during pregnancy, intrapartum, which is during the birth process, or post-partum, usually through breastfeeding. The risk of MTCT at any stage can be minimised with special interventions, including the provision of ART for pregnant women and mothers eligible for treatment. The WHO promotes a comprehensive strategic approach for the prevention of MTCT, which includes primary prevention of HIV infection among women of childbearing age, prevention of unintended pregnancies among women living with HIV, strategies of prevention of MTCT for woman living with HIV, and the provision of appropriate treatment, care and support to mothers living with HIV, their children and families. (WHO, 2010b:6,9). The program for the prevention of MTCT that is implemented globally under the guidance of the World Health Organisation (WHO), United Nations Children's Fund (UNICEF) and Joint United Nations Programme on HIV/AIDS (UNAIDS), is showing results in many areas and MTCT rates are decreasing rapidly (UNICEF, 2010:1).

Before 1985, the transfusion of blood and blood products was most commonly the mode of HIV infection in children. In developed countries infection through blood transfusion has efficiently been eliminated through improved screening tests, although in some developing countries screening is not as efficient (Rivera, 2012:Online).

2.2.2 HIV virology and immune system response

HIV is a virus with a spherical appearance and a diameter of approximately 110 nanometer (nm). The structure of the virus consists of a cylindrical core surrounded by a lipid bilayer envelope. The core contains the ribonucleic acid (RNA) genetic information that promotes viral replication and integration during initial cellular infection (Fisher *et al.*, 2007:3; McGovern *et al*., 2002:1712). Figure 2.1 is a schematic interpretation of HIV.

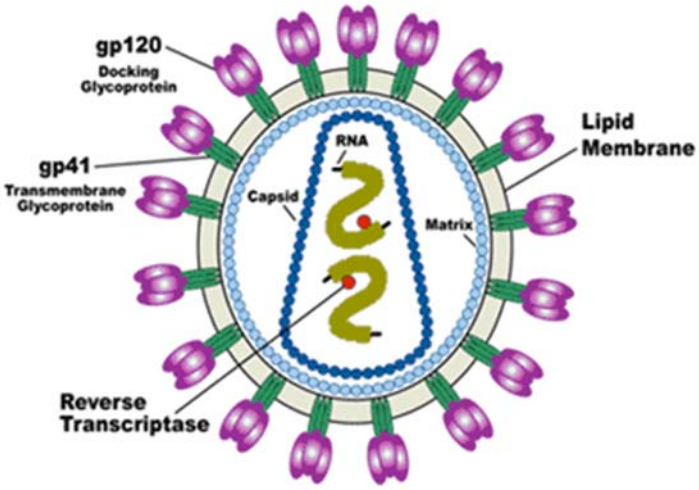


Figure 2.1: **Schematic interpretation of HIV (Montagnier, 1999:763)**

Viral infection occurs through the attachment of viruses to cells and subsequent penetration of the virus into the cell cytoplasm. Specific viruses target only specific cells. A variety of structural and non-structural proteins located on the surface of the target cell establish which cell types will be targeted by which viruses (Smith & Daniel, 2006:217).

HIV targets host T-helper cells (CD+ lymphocytes) and macrophages, which are key players in the human immune system. The immune system acts as the body's defence against all kinds of infections, including viral infections that cause disease. Invasion by HIV leads to destruction of the immune system, rendering the person unable to fight off both infectious and/or non-communicable ("diseases of lifestyle") diseases (Levy, 1993:183; Weiss, 1993:1273; Gilbert, 2003:573).

T-cells are responsible for the coordination of the immune system response to infection and to stimulate the production of T-cytotoxic and B-cells. The T-cytotoxic cells ingest and destroy all types of viruses and stimulate the production of B-cells. B-cells are responsible for the production of antibodies, which ingest and eliminate viruses (Chan & Kim, 1998:681; Fisher *et al.*, 2007:5; McGovern *et al*., 2002:1713).

In the case of HIV, the virus binds to the CD4+ protein and co-receptor on the surface of the T-cell, enabling the virus to enter the cell. Once inside the cell, viral reverse transcriptase (RT) copies the viral RNA to the host deoxyribonucleic acid (DNA). The viral DNA is transported into the nucleus of the host cell and incorporated into the host cell DNA. The virus then uses the host DNA profile to replicate itself. When the new viruses exit the host T-helper cells, the host cells are ruptured and in the process most of the host cells are killed (Levy, 1993:183; Weiss, 1993:1273; Fisher *et al.*, 2007:5; McGovern *et al*., 2002:1713).

In addition to the T-helper cells, HIV also infects macrophages and T-memory cells. These cells, together with some T-helper cells, are used to harbour viral particles, which will replicate over time to be dispersed to eventually infect other cells (Fisher *et al.*, 2007:5; McGovern *et al*., 2002:1713).

2.2.3 Stages and classification of HIV infection

HIV infection progresses through four stages, of which AIDS is the last stage. Figure 2.2 is a schematic interpretation of the progression of HIV infection to AIDS.

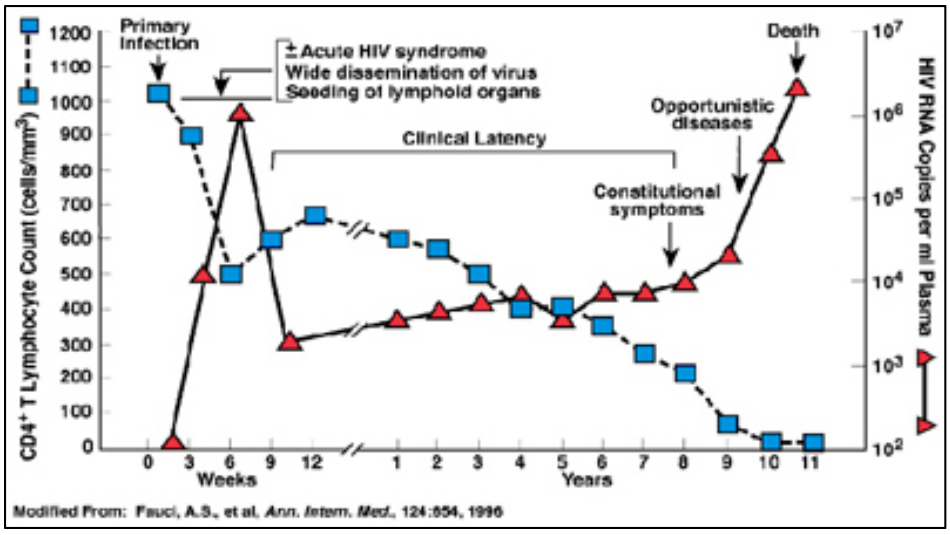


Figure 2.2: **Stages of progression of HIV infection (AIDSinfo:Online)**

The typical signs and symptoms seen at each stage of HIV progression have led to the development of clinical staging systems to describe the stage of HIV disease of an HIV-

infected person. In 1990, the WHO has developed a four-stage clinical staging system for HIV infection in adults (WHO, 1990:Online). In order to support the roll-out of ART to children, a three-stage system for children was proposed by the WHO in 2002 (WHO, 2003b:Online). After a series of regional consultations, studying of comments from public consultation and a global consensus meeting held in April 2006, the WHO published a revised four-stage clinical staging system and age-related immunological classification of HIV in 2007 (Table 2.1). This new document is especially helpful in the clinical management of HIV in areas where there is limited laboratory capacity. The WHO 2007 clinical staging system and immunological classification of HIV is in line with the four-stage clinical classification of the United States' Centers for Disease Control and Prevention (CDC) 1994 revised classification (WHO, 2007:3).

Table 2.1 WHO clinical staging and age-related immunological classification for established HIV infection.

HIV-associated immunodeficiency	WHO Clinical stage	Age-related CD4 values			
		<11 months (%CD4+)	**12-35 months (%CD4+)**	**36-59 months (%CD4+)**	**>5 years (absolute number per mm^3 or %CD4+)**
None or not significant	1	>35	>30	>25	>500
Mild	2	30-35	25-30	20-25	350-499
Advanced	3	25-29	20-24	15-19	200-349
Severe	4	<25	<20	<15	<200 or <15%
Adapted from WHO clinical staging of established HIV infection (WHO, 2007:12) and WHO immunological classification for established HIV infection (WHO, 2007:16)					

Clinical staging is used once HIV infection has been confirmed with serological and/or virological evidence. The clinical stage is useful for assessment at baseline and in the follow-up of patients in care and treatment programs. Clinical staging should be used to guide decisions on when to start co-trimoxazole prophylaxis and other HIV related interventions. It is also a useful tool to evaluate when to start antiretroviral therapy. The clinical stages

have been shown to be related to survival, prognosis and progression of clinical disease without antiretroviral therapy in adults and children (WHO, 2007:11).

2.2.3.1 Primary HIV infection

The first two to four weeks immediately after infection is referred to as primary infection or the acute phase. During this phase, the viral load rapidly increases and the person may experience symptoms of a mild to moderate viremia, characterised by fever, headaches, malaise, lymphadenopathy syndrome and/or pharyngitis. Symptoms such as orogenital ulcers and meningoencephalitis may be present, and the infected person may develop a maculopapular rash, which may last for a week up to a month. The virus can usually be detected with viral load tests about two weeks after infection. During this phase the person's ability to infect someone else is increased, because transmission of the virus is dependent on the viral load (WHO, 2007:11; Global Health Council:Online; Rivera, 2012:Online).

During this phase, the immune system reacts by developing antibodies to the virus. This process is known as seroconversion, and can take from one week to several months after initial infection. The number of T-cytotoxic cells increase, while the number of T-helper cells (specifically CD4+) in the blood decreases (Fenton & Silverman, 2008:996; Global Health Council:Online), although the number of CD4+ cells will still be above 500 cells/µl (CDC, 1994:Online). In adults, the development of antibodies and T-cytotoxic cells is associated with a slow-down in disease progression and a rapid decrease in viral load (Global Health Council:Online; Rivera, 2012:Online). In children, on the other hand, viral load rises faster and to higher values than in adults, and declines very slowly (Shearer *et al*., 1997:1337).

2.2.3.2 WHO clinical stage 1

After the primary or acute phase, the person enters a period known as the asymptomatic phase. During this phase few, if any, noticeable symptoms of HIV occur. In children persistent generalized lymphadenopathy may be present (WHO, 2007:17). The asymptomatic phase may last for many years, although most HIV-infected people start to

experience symptoms within 10 years (Fenton & Silverman, 2008:996; Global Health Council:Online; Rivera, 2012:Online). During this phase, the viral load remains low, thus the risk of transmission is also decreased. The number of T-helper cells increase and the levels of antibodies and T-cytotoxic cells stabilise. Antibodies are detectable in the blood (Fenton & Silverman, 2008:996; Global Health Council:Online; Rivera, 2012:Online). During this phase the number of CD4+ cells vary, but in adults and adolescents it can still be around 500 or more cells/µl (CDC, 1994:Online; WHO, 2007:16). In children older than five years of age the number of CD4+ cells/µl will also be 500 or more (WHO, 2007:16). In children younger than five years the CD4+ percentage is used to evaluate immunosuppression, and the value is dependent on age (Table 2.1).

2.2.3.3 WHO clinical stage 2

The reduction in cell-mediated immunity and secondary B-cell dysfunction result in the immunocompromised state and in the proliferation of opportunistic infections and malignancies. Mild symptoms of infection The reduction in the number of CD4+ cells circulating in the peripheral blood is closely inversely correlated with the plasma viral load. These two indicators are normally used as measures of disease progression. During this phase the number of CD4+ cells will be around 350 and 499 cells/µl in adults, adolescents and children older than five years of age (WHO, 2007:16). Table 2.1 gives an indication of the CD4+ cell percentages and degree of immunosuppression.

2.2.3.4 WHO clinical stage 3

Unexplained severe weight loss (>10% of presumed or measured body weight) in adults and unexplained moderate malnutrition or wasting that does not adequately respond to standard therapy in children are common symptoms of this stage. Other symptoms of this stage seen in adults as well as children include chronic diarrhoea, persistent fever, persistent oral candidiasis, oral hairy leukoplakia, pulmonary tuberculosis, severe bacterial infections (such as pneumonia, empyema, pyomyositis, bone or joint infection, meningitis or bacteraemia), acute necrotizing ulcerative stomatitis, gingivitis or periodontitis, unexplained

anaemia (<8 g/dl), neutropaenia (<0.5 × 109 per litre) or chronic thrombocytopaenia (<50 × 109 per litre) are symptoms of this stage.

This stage represents advanced immunodeficiency. During this phase the number of CD4+ cells will be around 200 to 349 cells/µl in adults, adolescents and children older than five years of age (WHO, 2007:16). In children younger than five years of age, the degree of immunosuppression is dependent on the age of the child (Table 2.1).

2.2.3.5 WHO clinical stage 4

The final phase is the phase where symptoms of AIDS develop. The viral load increases and the number of CD4+ T-cells decreases. The diagnosis of AIDS is dependent on the presence of at least one well-defined, life-threatening clinical condition that is linked to HIV-immunosuppression (Fenton & Silverman, 2008:996).

With regard to anthropometric nutritional status, HIV wasting syndrome is common in adults. In children, unexplained severe wasting, stunting or severe malnutrition that does not respond to standard therapy is common (WHO, 2007:16,18).

In adults and adolescents the CD4+ count will be less than 200 cells/µl (CDC, 1994:Online; WHO, 2007:16). In young children immunosuppression is experienced at a considerably higher CD4+ count (expressed and CD4+ percentage), due to the more aggressive nature of the infection in young children. This is demonstrated in the WHO immunological classification for established HIV infection (Table 2.1).

2.2.4 HIV/AIDS progression in children

Progression of HIV in children is different from that in adults, mainly because of the immaturity of a young child's immune system. Vertically transmitted HIV in children can cause rapidly progressive, chronically progressive or adultlike disease. Rapid disease progression within the first two years of life will generally occur in about 20% of children infected through MTCT. Some researchers estimate that 26% to 45% of African children

infected with HIV will die by their first birthday, and 35% to 59% by their second birthday. In the absence of ART, only a fraction will survive to the age of five years (Dabis & Ekpini, 2002:2097).

In infants and young children, viral loads decrease very slowly and often reach baseline levels only by the age of four or five years. The child's still immature immune system, with reduced cytokine production, proliferation and cytotoxicity, is not able to contain the viral infection. The young immune system is not able to develop significant numbers of precursors of cytotoxic T-lymphocytes (that are specific to HIV-1), until the age of 12 months. Envelope-specific cytotoxic T-lymphocytes are less common in children who vertically acquire the disease than in children who acquire HIV by means of blood transfusion. Among those with vertically acquired disease, lymphocytes are least common in those with rapidly progressing disease (Global Health Council:Online; Rivera, 2012:Online).

In a child with adultlike HIV, the child can be asymptomatic for many years. Growth failure, (defined as failure to grow according to standard growth charts), failure to reach developmental milestones within the expected time frame, frequent childhood illnesses, and sometimes brain or nervous system problems, can be indicative of HIV infection. Quite often it is only after the appearance of an opportunistic infection in a 10-year old child or an adolescent that the child is diagnosed with HIV infection. In turn, growth failure and the other symptoms mentioned in a patient with HIV infection may signify disease progression or underlying malnutrition (Benjamin *et al*., 2003:2331).

2.2.5 HIV/AIDS and mortality

Global mortality figures show that in developing countries, HIV/AIDS was the seventh leading cause of mortality in children in 2002. In 2004, more than 500 000 children under the age of 15 years died from HIV/AIDS. Due to the wider availability of anti-retroviral (ARV) medication, this number decreased to 380 000 in 2006 (UNAIDS, 2010b:8).

In Sub-Saharan Africa, which carries the largest burden of the HIV pandemic, the infant mortality rate has increased by 75% in areas affected by HIV/AIDS. This increase is partly

due to the orphaned status of most HIV-infected children in these areas. In many African countries, the mortality rates for children under the age of five years has increased to a point that is higher today than in 1990 – mostly because of the presence of HIV/AIDS (UNAIDS, 2010a:11). Preidis et al. (2011:484) noted that pneumonia and malnutrition are highly prevalent in HIV-infected and HIV affected children in Sub-Saharan Africa, and that these conditions were significantly associated with mortality in these children.

The Initial Burden of Disease Study carried out by the Medical Research Council of South Africa (MRC), has classified HIV/AIDS as the number one cause of death in children under five years of age in 2000. The percentage of under-five year olds who died of HIV/AIDS in that year was 35.1% of total deaths (Norman *et al*., 2006:Online).

2.3 CLINICAL MANIFESTATIONS OF HIV INFECTION

HIV infection has many health consequences, of which opportunistic infections are usually the first symptoms to appear. Other manifestations include malignant diseases, diseases of the liver, lungs (including tuberculosis), gastrointestinal tract, kidneys and the central nervous system. The impairment of the immune system due to the viral infection also increases the need for special attention to food, water and environmental hygiene.

2.3.1 Opportunistic infections

Children infected with HIV are prone to life-threatening opportunistic infections, of which the most common include infections with bacteria, fungi, protozoa, or viruses (Fenton & Silverman, 2000:897; NIAID:Online). Pneumonia, candidiasis and chronic diarrhoea are a few of the most common symptoms. The usual childhood infections occur more frequently and severely in children infected with HIV than in those not infected. The symptoms and side effects, which can include fever, seizures, recurrent colds, diarrhoea and dehydration (Fenton & Silverman, 2008:1008; NIAID:Online), often result in extended hospitalisation as well as nutritional problems (NIAID:Online) such as malabsorption and weight loss (Fenton & Silverman, 2000:899).

2.3.2 Malignant disease

Kaposi's sarcoma (KS) is a type of cancer that causes abnormal tissue growth under the skin. It is a common symptom of HIV/AIDS, although the use of ART has led to a decline in the number of cases of KS (Fenton & Silverman, 2008:1001). KS manifests as purple nodules on the skin, lymph nodes and mucous membranes or in the gastrointestinal tract (Grant, 2002:203). When situated in the mouth or oesophagus, KS lesions can cause pain and difficulty with chewing and swallowing. Diarrhoea and intestinal obstruction have been linked to KS lesions in the intestinal tract (Fenton & Silverman, 2008:1006).

Surgery, radiation therapy, and sometimes chemotherapy are used for the treatment of KS lesions (Fenton & Silverman, 2008:1006). Chemotherapy in itself, however, suppresses immune function, and should be used with caution in persons with already existing immune suppression (Fenton & Silverman, 2000:897).

Other malignant symptoms of HIV/AIDS include non-Hodgkin's lymphoma and Burkitt's lymphoma (Grant, 2002:203), which often affect the small bowel, causing malabsorption, diarrhoea, or intestinal obstruction. Impaired motor and cognitive abilities or change in personality are sometimes symptoms of primary lymphoma in the brain (Fenton & Silverman, 2000:897; Fenton & Silverman, 2008:1006).

2.3.3 HIV-liver disease

Infection with cytomegalovirus (CMV), cryptosporida, and hepatitis B, as well as the malignant diseases hepatic lymphoma and KS, often compromise liver function in HIV-infected patients (Fenton & Silverman, 2008:1006).

Infection with hepatitis C (HVC) is a common co-infection in HIV-infected persons, especially in those who are also injection drug users (Dong & Imai, 2012:868). HVC has been associated with accelerated progression of HIV disease and increased risk of cirrhosis (CDC, 2007: Online). This can affect the efficacy of HIV treatment, since impaired liver function will result in inefficient metabolism and excretion of ARV medication. Three classes of ARV

medications are associated with hepatotoxicity, complicating treatment with ARV medications (Lochet *et al.*, 2003:62; Dong & Imai, 2012:868).

2.3.4 Tuberculosis and lung diseases

Tuberculosis (TB), which is caused by *Mycobacterium tuberculosis,* is the most important cause of serious respiratory disease and common in persons infected with HIV. Co-infection with TB causes immune activation followed by a rapid increase in the rate of HIV replication in persons infected with HIV, and consequently faster progression to AIDS. *Mycobacterium tuberculosis* usually affects the lungs, but the disease may also occur in extrapulmonary sites. TB often infects the larynx, lymph nodes, kidneys, brain or bones of HIV-infected persons. In a person infected with HIV, the risk of TB infection is increased by medical conditions such as underweight (a body weight of 10% or more below ideal weight), the use of immunosuppressive therapy, and hematologic disorders, e.g. leukemia and lymphomas (Goletti *et al.,* 1996:2).

Pneumocystis carininii pneumonia (PCP) is common in HIV-infected infants in Sub-Saharan Africa, but rarely seen in adults in this region. The reason for this is not clear, since PCP is an important cause of death in HIV-infected adults in industrialised countries (Grant, 2002:201).

Although not all persons infected with *Mycobacterium tuberculosis* develop active TB, it has been found that those with both TB and HIV are 40 times more likely to develop active TB (Clum, 1996:51). In South Africa the combination of HIV and TB is one of the world's worst epidemics and indications are that it will get even worse, leading to increases in morbidity and mortality. The increase in multi-drug resistant (MDR) tuberculosis is adding an extra complication to the treatment of both these conditions (Karim et al., 2009:932).

2.3.5 Gastrointestinal problems

Chronic diarrhoea and sores in the mouth and oesophagus are the most common symptoms of the effect of HIV on the gastrointestinal (GI) tract.

The cause of chronic diarrhoea in HIV-infected persons is often not identifiable. In quite a number of cases protozoa and bacterial pathogens are the causes of diarrhoea (Grant *et al*., 2002:201). HIV/AIDS enteropathy is the term that is used to describe chronic, persistent diarrhoea in the absence of identifiable enteric pathogens (Fenton & Silverman, 2000:899). Atrophy of the villi is one of the symptoms of HIV/AIDS enteropathy and may be one of the causes of the persistent diarrhoea seen in HIV/AIDS patients (Fenton & Silverman, 2008:1006).

Candidiasis of the oral cavity and oesophagus are common in HIV patients worldwide. These lesions cause pain on chewing and swallowing, making it very difficult for the affected person to eat (Grant *et al*., 2002:201).

2.3.6 HIV-associated nephropathy

Deaths from kidney disease have increased in persons living with HIV/AIDS. The deaths seem to be as a result of a syndrome of progressive renal failure, referred to as HIV-associated nephropathy. HIV-infected patients with renal failure will need dialysis as well as adjustments in medication dosing and nutrition therapy (Fenton & Silverman, 2008:1006).

2.3.7 Neurologic symptoms

HIV enters the brain immediately after infection, often resulting in HIV encephalopathy, which often presents as a progressive dementia (Grant et al., 2002:202). A strong correlation has not yet been found between viral load in the brain and the level of neurologic decline. Other complications of the presence of the virus in the brain include myelopathy, peripheral neuropathy, and myopathy (Grant et al., 2002:203; Fenton & Silverman, 2008:1006).

Toxoplasma encephalitis, progressive multifocal leuko-encephalopathy, cytomegalovirus encephalitis, radiculomyelitis, cryptococcal meningitis (Grant et al., 2002:202), primary central nervous system (CNS) lymphoma, and neurosyphillis can lead to secondary neurologic complications (Fenton & Silverman, 2008:1006). These symptoms, which may

include partial paralysis, spasticity and weakness in the hands (Fenton & Silverman, 2008:1006), can have a significant effect on the ability of an HIV-infected person to maintain adequate nutrition.

Due to the neurologic symptoms of HIV infection, children infected with HIV are often slow in reaching important milestones in motor skills and mental development, e.g. crawling, walking and talking. As the disease progresses, many children develop neurologic problems such as difficulty walking, poor school performance and symptoms of HIV encephalopathy (UNICEF, 2010:1-12).

2.3.8 Other concerns related to nutrition

Immune suppression, a symptom of HIV infection, increases the vulnerability of HIV-infected persons to food- and water-borne pathogens. Food and water safety need to be given priority by persons infected with HIV, as well as in communities where people are living with HIV. Food and water hygiene and safety practices must be taught to HIV-infected patients, and practiced at home as well as when eating out or traveling (Fenton & Silverman, 2000:907).

2.4 THE RELATIONSHIP BETWEEN MALNUTRITION AND HIV/AIDS

Nutritional status and malnutrition in HIV-infected persons are closely interrelated. Nutritional status is an important predictor of disease progression and survival in HIV-infected persons (Preidis, 2011:488), while at the same time HIV infection negatively affects nutritional status (Benjamin *et al*., 2003:2332).

Malnutrition refers to both over- and undernutrition. In this document malnutrition will imply undernutrition. Undernutrition develops when nutritional reserves are depleted or food intake is inadequate to meet daily metabolic needs. Undernutrition often results in impaired growth and development in young children, as well as lowered resistance to infection, poor clinical outcome from disease, development of chronic disease and increased morbidity and mortality. These symptoms are often worse in HIV-infected

children. Malnutrition in HIV-infected persons leads to immune dysfunction, which in turn increases the frequency and severity of opportunistic infections (Semba & Tang, 1999:182). The infections in turn contribute to further malnutrition, causing a vicious cycle of infection, illness, malnutrition, more infection, more malnutrition (Figure 2.3).

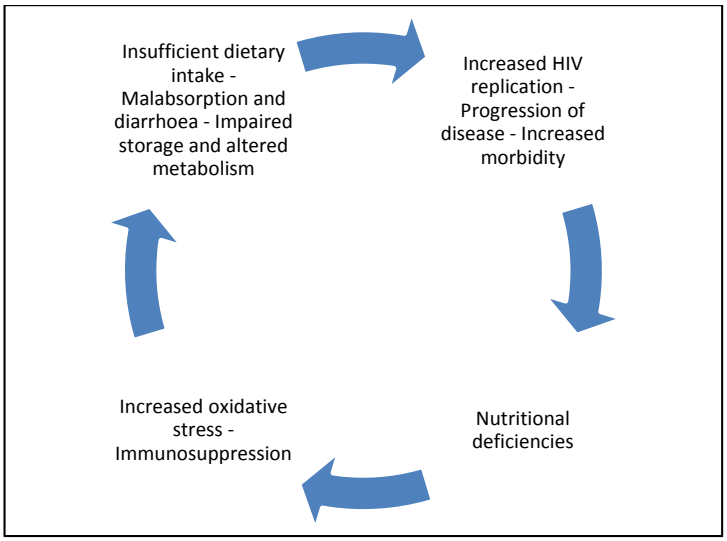


Figure 2.3: The vicious cycle of malnutrition and HIV (Semba & Tang, 1999:182)

The most frequently reported symptoms of malnutrition in HIV-infected persons and in those with HIV/AIDS, include severe weight loss, depleted body cell mass, marked decrease in skinfold thickness and mid upper arm circumference measurements, decreased iron-binding capacity, and hypoalbuminemia (Collins, 1988:22). Nutritional deficiencies that are commonly identified in HIV-infected persons include deficiencies of protein, energy, essential fatty acids, mineral elements copper, zinc, selenium and iron, pyridoxine, and vitamins A, C and E and folate. These deficiencies all exert some form of detrimental effect on immune function (Fenton & Silverman, 2008:1009).

Severe weight loss in HIV-infected persons is known as HIV/AIDS wasting syndrome. The CDC defines HIV/AIDS wasting syndrome as “profound involuntary weight loss of more than 10% of baseline body weight plus either chronic diarrhoea (two loose stools per day for more than 30 days) or chronic weakness and documented fever (for 30 days or more, intermittent or constant), in the absence of a concurrent illness or other condition that would explain the symptoms” (Fenton & Silverman, 2008:1008). In persons with HIV/AIDS,

involuntary loss of 10% to 15% of body weight is common. Weight loss is an important predictor of survival in HIV (Knox *et al*; 2003:S63; Villamor *et al*., 2005:61; Tang & Kaslow, 2003:S27; Zachariah *et al*., 2002:293; Fenton & Silverman, 2008:1008). A loss of as little as 5% of body weight has been associated with a significantly increased risk of opportunistic infections and death (Wheeler *et al*., 1998; Wanke, 2004:S279), while a loss of more than 10% is associated with a four- to six-fold greater risk (Harrison, 2010:6). Organ damage caused by severe weight loss can also add to the increased risk of death from infections (Fenton & Silverman, 2008:1008; Heller *et al*., 2000:323, Knox *et al*., 2003:S68).

The added demands of growth and development on nutrition put the nutritional status of HIV-infected children even more at risk than in the case of adults (WHO, 2003a:3-4; Bunn *et al*., 2009:108; Preidis, 2011:488). Growth failure and weight loss are the most prevalent systemic manifestations of HIV infection in children (Semba & Tang, 1999:182). Up to 94% of HIV-infected children have been identified with stunting and growth failure (Fenton & Silverman, 2000:894).

Growth in height is also affected in the majority of children infected with HIV. Deficient linear growth (height-for-age) is known as stunting. Stunting is strongly associated with disease progression and early mortality. In children with slow disease progression, stunting could be identified earlier and more pronounced than a decrease in weight-for-age (Bobat *et al*., 2001:205; Kimani-Murage *et al*., 2011:23; Ramalho *et al*., 2011:454; Steenkamp *et al*., unpublished). In children with rapidly progressive disease, stunting was combined with wasting (Bobat *et al*., 2001:206). Villamor *et al*. (2005:61-68), found that the risk of death among children who were stunted was twice as high of the risk of children who were not stunted.

2.5 MALNUTRITION IN HIV-INFECTED CHILDREN

Several factors associated with HIV infection can contribute to the development of malnutrition. The disease process influences the food intake of an HIV-infected person, which in turn influences the nutritional status and health of the individual. The majority of people infected with HIV live under poor socio-economic conditions, which have a further

negative impact on food intake, nutritional status and health. Children are even more vulnerable than adults to the impact of these factors, due to their less developed immune system and their relative high nutritional needs for proper growth and development.

2.5.1. HIV/AIDS disease process

HIV infection increases the nutritional needs of HIV-infected patients. Symptoms caused by opportunistic infections lead to reduced oral intake and/or nutrient malabsorption, with a consequent negative impact on nutritional status. These factors all complicate efforts to maintain ideal nutritional status and growth in HIV-infected children.

Increased energy expenditure is regarded as to be one of the main causes of weight loss in people infected with the HIV. People infected with HIV require approximately 10% more energy while resting, compared to those who are uninfected. This figure seems to be even higher in people with advanced infection or AIDS, as well as in children infected with HIV (WHO, 2003a:3,4).

The food and nutrient intake of children infected with HIV needs to make provision for the increased needs over and above the needs for normal growth and development. Inability to meet these increased nutritional needs result in malnutrition, which in turn will lead to the progression of HIV disease (Semba & Tang, 1999:182).

2.5.2.1 Reduced food intake

Reduced food intake is the most prominent factor leading to wasting and malnutrition in HIV-infected children (ADA, 2000:432; Cant *et al*., 2003:1305). Symptoms of HIV infection, such as loss of appetite and painful sores in the mouth, can contribute to reduced oral intake (Fenton & Silverman, 2008:1008).

The presence of HIV infection as well as the medications used, can lead to symptoms such as nausea, vomiting, diarrhoea, dyspnea or fatigue, which can cause a loss of appetite and decreased food intake. Neurologic disturbances (e.g. HIV encephalopathy), and physiological

factors such as depression, are common in HIV-infected individuals and can also cause loss of appetite (Fenton & Silverman, 2008:1008) with subsequent insufficient intake of food.

Painful sores in the mouth, pharynx or esophagus (Rabie et al., 2007; Fenton & Silverman, 2008:1008), caused by Kaposi lymphoma (Fenton & Silverman, 2000:879) or by oral candidiasis (Fenton & Silverman, 2008:1008) can inhibit normal chewing and swallowing and lead to reduced food intake (Fenton & Silverman, 2000:879).

The amount of food eaten can also be influenced by characteristics of the food itself, especially in the case of starch-based staple foods. Starch-based staple foods often contain dietary bulk, have a high viscosity and low energy density, which makes it difficult for a child to meet energy needs (Den Besten *et al*., 1998:4). This is a challenge especially for a sick child with diminished appetite.

2.5.2.2 Nutrient malabsorption due to diarrhoea and opportunistic infections

Diarrhoea, mostly caused by opportunistic infections, is the major nutritional problem experienced by HIV-infected persons, and often the most difficult problem to resolve (Fenton & Silverman, 2000:899).

Diarrhoea is a common symptom of HIV infection in at least 50% of all persons infected with HIV. HIV-infected persons with a CD4+ count of less than 200 to 250 cells/mm^3 are at the greatest risk of developing diarrhoea (Fenton & Silverman, 2000:906). Children infected with HIV appear to be especially vulnerable to diarrhoeal diseases, which contributes significantly to poor growth and is strongly associated with increased mortality (Bunn *et al*., 2009:108). A newly acquired intolerance to lactose, fat, and in some cases gluten, can also be a cause of diarrhoea (Miller *et al*., 1991:1300; Fenton & Silverman, 2008:1008).

Malabsorption is a common result of diarrhoea in patients infected with the HIV. Malabsorption can also be caused by small-bowel bacterial overgrowth due to gastrointestinal dysmotility or hypochlorhydria, and may also predispose the child to malabsorption (Miller, 2003:S134). Malabsorption of fats, monosaccharides, disaccharides,

nitrogen, vitamin B12, folate, minerals and trace elements are common manifestations of bacterial infection of the small bowel. Infection of the large bowel results in malabsorption of fluids and electrolytes (Fenton & Silverman, 2000:906). Malabsorption can be aggravated by opportunistic infections that affect the hepatobiliary system and pancreas (Miller, 2003:S134).

2.5.2 Socio-economic factors and their influence on nutritional status of children infected with or affected by HIV

Social and socio-economic factors that influence food availability and the quality of the diet play an important role in the dietary intake of children and can have a specifically negative impact on the nutritional status of HIV-infected as well as HIV affected children.

Children born into households where the mother or father (or both) are infected with HIV, are at risk of losing one or both parents early in life, with resultant socio-economic consequences on the health and wellbeing of the orphaned child.

2.5.2.3 The role of social and organisational structures in food availability and in the development of malnutrition

The relationship between food, malnutrition and health is complex and depends on a variety of factors, including the role of social and organisational structures in the community. Figure 2.4 illustrates the conceptual framework developed by UNICEF for understanding the causes of malnutrition. The causes of malnutrition can be classified into three main levels:

a) Basic causes, which involve entire societies.
b) Underlying causes, that involve households and communities
c) Immediate causes, which involve the individual

The basic (or indirect) causes of malnutrition relate to the community or the nation, and refer to the effectiveness of management of human-, economic- and organisational resources, including political and economic structures. The availability and standard of

education rendered by the government also plays a key role in the basic causes of malnutrition. When these structures are mismanaged or not used effectively, they contribute largely to the development and prevalence of malnutrition.

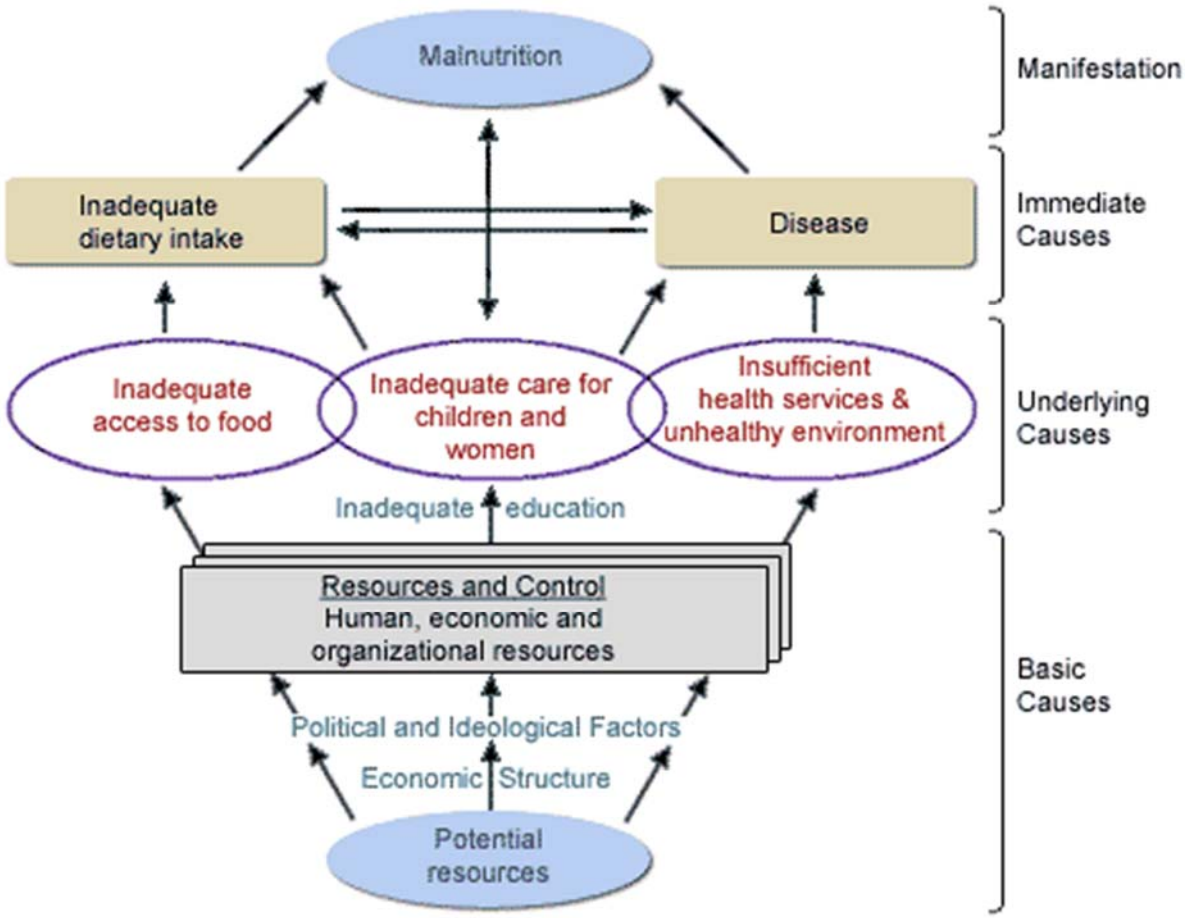


Figure 2.4: **The UNICEF conceptual framework of malnutrition (Council for Agricultural and Rural Development, 2011:Online)**

The underlying causes of malnutrition relate to families and family structures, and specifically household food security. Household food security is defined as sustainable access to sufficient quantities of safe, good quality food to ensure a balanced, adequate dietary intake and a healthy life for all members of the family (UNICEF, 1998:Online).

A lack of household food security leads to inadequate dietary intake. A number of factors can negatively influence household food security, e.g. lack of resources in terms of money to buy food, and in terms of knowledge, skills and time to purchase and/or produce food, and

prepare healthy meals. Poor dietary intake can also be the result of illness accompanied by lack of health care due to ignorance, insufficient health services or inability to make use of health services. In the case of children, poor food intake can be due to illness of the child carer. As an example, in a household of low socio-economic status, food availability will be negatively affected. Illness of the mother or child carer will further decrease food availability to the young child, because the mother is likely to be too ill or just not feeling well enough to prepare food and feed the child (Kikafunda & Namusoke, 2006:7; Mangili et al., 2006: 836; Collins & Leibbrandt, 2007:S75; Bunn, 2009:108). Poor health and poor emotional and psychological status of the mother, as well as an insupportive caregiver-child interaction all can have a negative influence on child growth (UNICEF, 2006:Online).

Inadequate food intake and disease are the immediate causes of poor nutrition in an individual, mostly because of decreased immunity that leads to infections. Figure 2.3 describes the vicious cycle where low immunity leads to infection, infection leads to malnutrition, malnutrition in turn leads to further infection, causing the problems to intensify and manifest as malnutrition. The negative impact on the nutritional status of the population increases in size and severity as the indirect causes increase in number and intensity (UNICEF, 1998:Online).

2.5.2.4 Socio-Economic implications for children orphaned by HIV/AIDS

HIV/AIDS has created a new category of highly vulnerable households, namely those with ill adults (parents) or where one or both parents have died due to HIV/AIDS. Children who have lost one or both parents due to HIV/AIDS or HIV/AIDS related illness, known as HIV/AIDS orphans, are even more vulnerable with regard to loss of household food security, financial hardship, ill health and negative socio-economic influences in their life. The death of the father or head of the household due to HIV/AIDS often results in woman-headed and even child-headed households, where neither the mother or the child is capable or educated sufficiently for the responsibility, and at the same time the household has lost its main, or often, only income (Mishra *et al*., 2005:6; UNICEF, 2006:2; UNAIDS, 2010b:186). Young children have to take responsibility to care for younger siblings, or possibly even for the longer living parent, who might also be ill or even bedridden. Often these children also

have to deal with issues of being relocated to other family while they are still mourning the death of a parent (Kikafunda & Namusoke, 2006:7; Collins & Leibbrandt, 2007:S75; Bunn, 2009:108).

2.6 ANTHROPOMETRIC NUTRITIONAL STATUS AND GROWTH

Growth is measured by using anthropometric measurements of the body. Except for weight and height, measurements of head circumference, mid upper arm circumference and skinfold thickness can also be used. These measurements can be used to evaluate anthropometric nutritional status by evaluating the measurements of an individual against specific standards of growth for each type of measurement used.

2.6.1 The International Reference Population

Growth standards or references are parameters that are used to assess nutritional status through the use of anthropometry. Growth standards or references consist of growth charts as well as anthropometric tables that are useful tools for the assessment of children's anthropometric nutritional status. It can also be used by government institutions and United Nations (UN) agencies to measure the general well-being of populations, formulate health and related policies, plan interventions and monitor their effectiveness.

The two main standards of reference available for the measurement of anthropometric nutritional status are the National Centre for Health Statistics (NCHS) Growth Reference Guide and the WHO Growth Standards.

The NCHS Growth Reference Guides have been used internationally and are based on data from many cross-sectional and a few longitudinal studies that have been incorporated into a variety of charts and tables, depicting relationships of weight, height and age (Hamill *et al*., 1979:608). Although this was useful, it had weaknesses. These reference guides were based on data from small, biased study samples with inherent limitations that made it less suitable for application to the general population (Hamill *et al*., 1979:607). The NCHS reference guides have, however, been updated with new data, mainly from the third National Health

and Nutrition Examination Survey (NHANES III). The study population for the NHANES III study did include a more complex sample than the earlier surveys used as basis for the NCHS Reference Guides, making the revised reference guides more suitable for a multi-cultural population. The revised growth charts and tables for children ranging from two to 20 years have been published in 2000 by the CDC (Frisancho, 2008:204). These revised growth charts and references are known as the CDC 2000 growth charts and references.

The WHO has also constructed their own growth standards which are more suitable for multi-cultural settings. The WHO standards were published in 2006 (WHO, 2006b). According to the WHO, some of the biggest limitations of the NCHS Growth Reference Guide and the CDC 2000 growth charts, were that the data used to construct the reference covering birth to three years of age came from a group that was not representative of the international community, were not weighed frequently enough to describe the rapid and changing rate of growth in early infancy, and were not fed according to updated WHO recommendations (WHO, 1994:42-43).

In 1994 the WHO requested that an expert committee revise the available growth references and make suitable recommendations for the assessment of anthropometric nutritional status of children. The conclusion was that the NCHS growth reference was not totally suitable for under-fives. The WHO Expert Committee recommended the development of a new international growth reference for infants and children from birth to five years (WHO, 1994:42-43; Gibson, 2005:299). To obtain data for the WHO reference standards, a WHO Multicentre Growth Reference Study (MGRS) was carried out between 1997 and 2003. More than seven diverse geographic areas were represented, namely North and South America, Europe, Sub-Saharan Africa, eastern, southern and western Asia (Garza & De Onis, 1999:171S).

The MGRS was purposely designed to produce a standard rather than a reference. Standards and references can both serve as a basis for comparison, but it is important to remember that each enables a different interpretation. A standard defines how children should grow rather than merely describing how they grew at a particular time and place (Garza & De Onis, 2004:S12). In order to develop a standard, the sample for the MGRS was

different from the sample used in the studies on which the NCHS Reference Guide is based. For the MGRS, healthy, privileged children living under conditions likely to favour achievement of their full genetic growth potential was used in the sample. Only children of mothers who engaged in fundamental health-promoting practices, e.g. breastfeeding and complying to WHO feeding recommendations, were selected for the sample for construction of the standards. Mothers who engaged in activities that could negatively impact the growth and development of their children, e.g. smoking, were excluded from the study. Anthropometric measurements of children in the sample were taken monthly (De Onis *et al*., 2004:S15-26). In contrast, the NCHS data is based on three-monthly anthropometric measurements of infants and children predominantly from middle-class families, and of whom the majority were fed proprietary formula-based products (De Onis *et al*., 2004:S15-26).

Growth standards and growth references are not interpreted in the same way. Deviations from the pattern of growth described by growth standards can be interpreted as evidence of abnormal growth. In the case of a growth reference, such value judgments cannot always be made. It is important to make sure that in practice references are not mistakenly used as standards (De Onis and Blössner, 1997:Online; De Onis *et al*., 2004:S15-26).

2.6.3 Anthropometric measurements of nutritional status in children

2.6.2.1 Weight/height status

The use of measurements of weight and height and changes in weight and height is fast and uncomplicated and an effective way to assess anthropometric nutritional status. Weight and height can be interpreted as weight-for-age, height-for-age, weight-for-height or as BMI-for-age.

(iv) Weight-for-age

Weight is relatively easily measured, and is therefore commonly used when the child's age can be accurately determined. Weight-for-age (W/A) reflects body weight relative to a

child's age on a given day. W/A can be used to evaluate whether a child is underweight, but it is not used to diagnose overweight or obesity (WHO, 2008:5). W/A is influenced by both the height and weight of the child, which makes interpretation complex (Benjamin *et al*., 2004:702 Gibson, 2005:254), because a child may be underweight either because of short length/height (stunting) or thinness or both (WHO, 2008:5). W/A can thus not distinguish between short children of adequate body weight and tall, thin children. W/A is however invaluable for routine assessment of growth and is the most effective measurement to identify acute changes (Benjamin *et al*., 2004:702 Gibson, 2005:254).

W/A can be misinterpreted in cases where a severely malnourished child has oedema. Fluid retention increases weight, subsequently masking very low weight. It is therefore important to check for the presence of oedema when weighing a child, especially if the child appears to be ill (WHO, 2008:5).

(v) Length/height-for-age

Length/height-for-age (H/A) reflects attained growth in length or height at a specific age. H/A can help identify children who have short stature for age or a process of failure to reach linear growth potential (WHO, 1997:46), known as stunting (WHO, 1997:46; WHO, 2008:3). Stunting is a result of continuous undernutrition and/or repeated illness over a significant period of time (Gibson, 2005:256; WHO, 2008:3). Children who are tall for their age can also be identified by using H/A, but tallness is rarely a problem. Excessive tallness may sometimes reflect uncommon endocrine disorders (WHO, 2008:3).

A high prevalence of stunting in populations is often the result of poor socioeconomic conditions. It also reflects an increased risk of frequent and early exposure to infavourable conditions, e.g. illness, often combined with inappropriate feeding practices (WHO, 1997:46).

(vi) Body mass index-for-age

Body mass index (BMI) is calculated using a person's weight and height. BMI can be used as an indicator of body fatness for most children and adolescents. BMI does not measure body fat directly, but it does correlate to direct measures of body fat, such as underwater weighing. BMI is an inexpensive and easy-to-perform method of screening for weight categories that may lead to health problems. For children and adolescents, BMI is age- and gender-specific and is therefore referred to as BMI-for-age (BMI/A) (CDC, 2011:Online).

The new WHO Growth Standards as well as the updated CDC 2000 growth charts include BMI/A as a reference to evaluate a child's weight in comparison to the weight of a refence population.

BMI is in effect an adjusted evaluation of weight-for-height, where in the case of BMI weight is adjusted for height or length (Benn, 1971:42). BMI is a useful tool for comparisons of weight between adults of different lengths, without the need to take age in consideration. In the case of children, however, BMI is age specific and the use of BMI/A is recommended (Lee & Nieman, 2010: 168; Ogden *et al*., 2002:78). BMI or BMI/A does not evaluate adiposity. In the case of high or low BMI or BMI/A values, BMI or BMI/A must be evaluated in conjunction with measurements that can evaluate the percentage of body fat, e.g. skinfold thickness (Frisancho, 2008:318).

2.6.2.2 Head circumference

Head circumference (HC), or frontal occipital circumference (FOC), changes most rapidly during the first two years of life, and during this time the measurement of HC is a useful tool to monitor child brain growth (Gibson, 2005:254; Frisancho, 2008:313; Lowenthal & Phelps, 2009:255). Head circumference-for-age (HC/A) can be used as an index of chronic protein-energy malnutrition in children younger than two years. After the age of two years, growth in HC is too slow to be a useful measurement of growth or nutritional status (Gibson, 2005:254).

HIV infection in young children can result in reduced brain growth and development (Gibson, 2005:254) because the brain is one of the primary targets of HIV (Fenton & Silverman, 2008:1006). Delayed growth in HC is correlated with the development of underlying encephalopathy (Fenton & Silverman, 2008:1006). Normal head growth on the other hand, does not help in ruling out encephalopathy, and many patients with a normal HC may have radiographic or psychometric findings consistent with encephalopathy (Rivera, 2012:Online). Research could not establish a statistically significant difference in HC at birth between HIV-infected and non-infected children yet. A trend toward smaller HC in HIV-infected children was found in the Women and Infants Transmission study (WITS) (Moye *et al*., 1996:62).

Based on the above, Lowenthal and Phelps (2009:255) suggest that HC can be used, together with weight and length, as a tool for the identification of infants at risk for unfavourable outcomes.

2.6.2.3 Upper arm anthropometry

(v) Mid upper arm circumference

Mid upper arm circumference (MUAC) has been found to be particularly useful in the diagnosis of protein-energy malnutrition or starvation in developing countries. MUAC measurements can also be used to monitor progress during nutrition therapy (Gibson, 2005:290).

Measuring the MUAC provides a useful tool to identify a child with wasting syndrome. Since the arm contains both subcutaneous fat and muscle; a decrease in MUAC can be interpreted as a reduction in either muscle mass or subcutaneous tissue or both (Gibson, 2005:290). The loss of weight in an HIV-infected child will reflect as a low MUAC for age, as the child loses subcutaneous fat and muscle mass (Lowenthal & Phelps, 2009:259). It is important to keep in mind that the presence of oedema can make the MUAC appear falsely elevated (Lowenthal & Phelps, 2009:255).

(vi) Triceps skinfold thickness

Skinfold thickness measurements provide an estimate of the size of the subcutaneous fat depot. These measurements can be used for calculations of an estimate of total body fat or percentage of body fat.

Skinfold thickness can be measured at different sites, e.g. triceps, biceps, subscapular, suprailiac and midaxillary (Gibson, 2005:274-5). The use of skinfold thickness measurements from a combination of sites usually gives a more accurate estimate of total body fat, because subcutaneous fat is not uniformly distributed through the body. When a skinfold thickness measurement from a single site is used to estimate total body fat or percentage body fat, selection of the skinfold site that is most representative of the whole subcutaneous fat layer is critical (Gibson, 2005:277). Whether total body fat or percentage body fat will be evaluated, also determines which skinfold site should be selected.

The use of single skinfold measurement sites to estimate percentage of body fat is difficult. Roche *et al*. (1981:2831) found that in cases where limited skinfold measurements are available, triceps skinfold (TSF) measurements provided the best estimate of percentage body fat (Lee & Nieman, 2007:194) in women and children (Gibson, 2005:278). Single-site measurements of TSF can be used to make comparisons among subjects in a study population (Lee & Nieman, 2007:197). Due to its accessibility, TSF is the skinfold measurement that is most frequently selected for a single, indirect estimate of body fat. However, it is only suitable for use as a single site of measurement in women and children (Gibson, 2005:278; Lee & Nieman, 2007:194). A negative aspect is that the process of measuring TSF is unpleasant for young children, which can influence the accuracy or availability of measurements (in cases where a child totally refuses that the the TSF is measured). TSF does, however, provide valuable data in research studies (Shaw & Lawson, 2007:7).

(vii) Upper arm muscle area

Measurements of the MUAC and TSF are used to calculate the upper arm muscle area (UAMA). The UAMA is an estimation of the area of the bone and muscle portions of the upper arm (Frisancho 2008:314). UAMA can be used to assess total body muscle mass. Since muscle mass is an index of protein reserves, UAMA can reflect muscle tissue changes and can be used as an indication of protein energy malnutrition (PEM) (Gibson, 2005:292).

Brachium radiographic shadow is the technique used to compute upper arm areas. The technique was originally used by Baker *et al*. in 1958 (Frisancho, 2008:19). The technique assumes that the upper arm and its constituents are cylindrical. The corresponding areas of cross section are computed from the formula that yields the areas of a circle from its circumference (Frisancho, 2008:19). The calculations are done using the following formulas:

Letting C equal the circumference of the upper arm, the total area is calculated as (Frisancho, 2008:19):

Total upper arm area (TUA) = $(C^2)/(4 \times л)$
UAMA = $\{C – TSF \times л)^2/(4 \times л)$

(viii) Upper arm fat area

Measurements of the MUAC and TSF are used to calculate the upper arm fat area (UAFA). The UAFA is an estimation of the area of the fat portions of the upper arm (Frisancho 2008:314). UAFA is calculated using the following formula (Frisancho, 1990:21; Frisancho, 2008:19):

UAFA = (Total upper arm area – upper arm muscle area)

UAFA can also be used to derive an estimate of total body fat. This calculation provides a more accurate estimate of total body fat than a single skinfold at the same site. The use of this value does, however, have its limitations. The equation assumes that the limb is

cylindrical, with fat evenly distributed about its circumference, without making allowance for differences in skinfold compressibility, which will have an influence on the accuracy of total body fat estimates (Gibson, 2005:294).

2.6.4 Classification of anthropometric nutritional status/growth disorders

Three different systems can be used to compare a child or group of children to the reference population: Standard Deviation (SD) or Z-scores, percentiles, and percent of median.

2.6.4.1 Z-score

The Z-score is the most widely used and useful system for analysis and presentation of population-based assessments. Z-score expresses the anthropometric value as a number of SD units or Z-scores below or above the reference mean or median value (Benjamin *et al*., 2004:702; WHO, 2008:46; Frisancho, 2008:303).

The advantages of using Z-scores are:

- Z-scores are comparable across ages, groups and indicators, e.g. a reference limit of -2 Z-scores represents the same degree of malnutrition, irrespective of the anthropometric index used or the age of the child.
- Z-scores are gender independent, sex and age groups can therefore be combined for evaluation of children's growth status.
- The characteristics of Z-scores allow further computation of summary statistics (means, SD, standard error) to classify a population's growth status (Benjamin *et al*., 2004:702).

The use of Z-scores is recommended by the WHO for evaluating anthropometric data from low-income countries. Z-scores can be calculated accurately beyond the limits of the reference data, making it possible to classify persons with indices below the extreme percentiles of the reference data accurately (Gibson, 2005:337).

A Z-score cut-off point of <-2 SD is used by the WHO Global Database on Child Growth and Malnutrition to classify low weight-for-age, low height-for-age and low weight-for-height as moderate and severe undernutrition. The cut-off for severe undernutrition is <-3 SD. Overweight in children is classified by a cut-off point of >+2SD. Table 2.2 provides a summary of WHO definitions of growth problems in terms of Z-scores.

Table 2.2 WHO classification of anthropometric nutritional status using Z-score values (WHO, 2008:14)

Z-score	Growth indicators			
	Length/height-for-age	Weight-for-age	Weight-for-length/height	BMI-for-age
Above 3	*See note 1*	*See note 2*	*Obese*	*Obese*
Above 2			*Overweight*	*Overweight*
Above 1			*Possible risk of overweight (See note 3)*	*Possible risk of overweight (See note 3)*
0 (median)				
Below −1				
Below −2	*Stunted (See note 4)*	*Underweight*	*Wasted*	*Wasted*
Below −3	*Severely stunted (See note 4)*	*Severely underweight (See note 5)*	*Severely wasted*	*Severely wasted*

Notes:

1. *A child in this range is very tall. Tallness is rarely a problem, unless it is so excessive that it may indicate an endocrine disorder such as a growth-hormone-producing tumor. Refer a child in this range for assessment if you suspect an endocrine disorder (e.g. if parents of normal height have a child who is excessively tall for his or her age).*
2. *A child whose weight-for-age falls in this range may have a growth problem, but this is better assessed from weight-for-length/height or BMI-for-age.*
3. *A plotted point above 1 shows possible risk. A trend towards the 2 z-score line shows definite risk.*
4. *It is possible for a stunted or severely stunted child to become overweight.*
5. *This is referred to as very low weight in IMCI training modules. (Integrated Management of Childhood Illness, In-service training. WHO, Geneva, 1997).*

A Z-score can be explained using the concept of a normal distribution. In a normal distribution, the distribution of measurements around the median is symmetrical, with most

of the values grouped around the middle values (Figure 2.5). In a normal (symmetrical) distribution, a z-score gives an indication of how far a child is from the median for the anthropometric measurement evaluated.

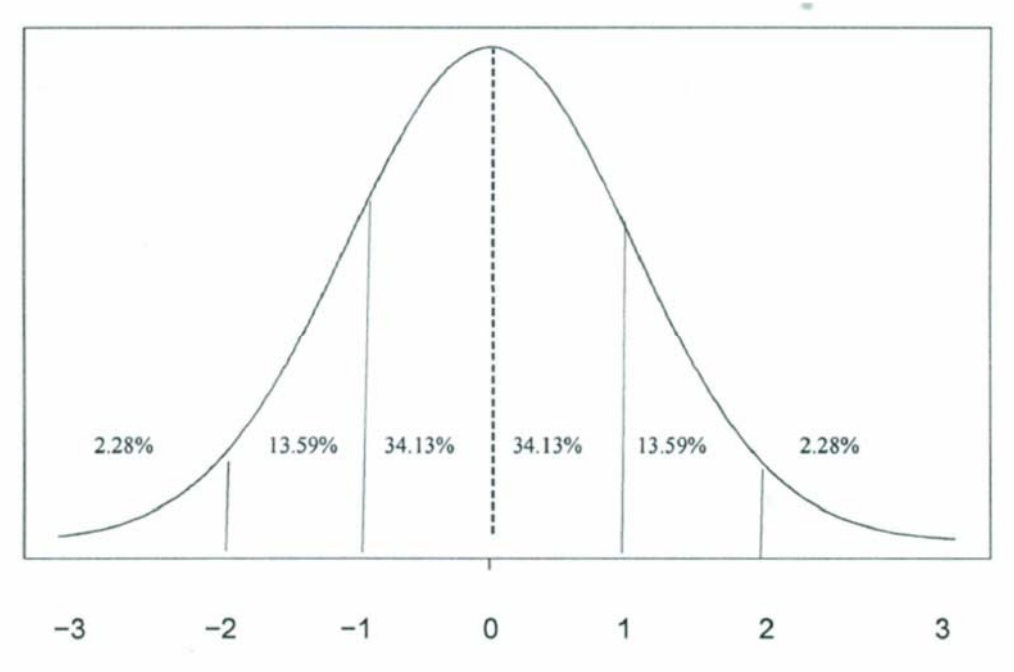


Figure 2.5 A normal distribution curve cut into z-score segments (WHO, 2008:46)

Anthropometric measurements of a reference population can either be distributed normally (symmetrical) or non-normally (asymmetrical). Two different formulas are used for calculation of Z-scores for measurements that are distributed normally and for measurements that are distributed asymmetrical. The use of the two formulas is demonstrated in Example 1 and Example 2 respectively.

The distribution of height-for-age in a population of boys or girls in the same age group will resemble the normal distribution in Figure 2.5. Most of the heights are in the middle, with very few at the extreme ends. Each segment on the horizontal axis represents one standard deviation or z-score. In a normal distribution, the value of the median is zero, and is in the centre of the bell shape. The z-scores -1 and 1 are at equal distances in opposite directions from the median. The distance from the median to 1 is equal to the distance from 1 to 2. In this distribution, 2.28% lies between -2 and minus infinity, and between +2 and plus infinity (WHO, 2008:46). This implies that 2.28% (rounded to 2.3%) of the reference population will

be classified as malnourished even if they have no growth impairment, and that 2.28% (2.3%) of the population can be regarded as the baseline or expected prevalence. Further, if the proportion below -2 in the study population is significantly larger than 2.28%, it implies that the study population is more severely affected than the reference population (Gibson, 2005:338).

The z-score of an observed point in the normal distribution is calculated using the following formula:

$$\text{Z-score} = \frac{\text{(observed value) - (median reference value)}}{\text{z-score of the reference population}}$$

Example 1

As an example, the formula for data with a normal distribution is applied to height-for-age in children to calculate the height-for-age Z-score (HAZ) of a boy who is 96.1 cm tall and 2 years and 4 months old:

- The observed value is the boy's height (96.1 cm).
- The median reference value is the median height measured of all boys in the same age group as the boy in the example (2 years and 4 months). The median height of boys in the age group 2 years and 4 months is 90.4 cm.
- The z-score of the reference population can be described in a simplified way as an average of differences from the median for each member of the reference population. In this example, the z-score of boys' heights at age 2 years and 4 months is 3.3.
- Using the above values in the formula, the boy's z-score is calculated as follows:

$$\text{Z-score} = \frac{96.1 - 90.4}{3.3} = 1.73$$

- This boy's z-score for height-for-age is 1.73, or above 1.

A Z-score for height-for-age of above 1 for the boy in the example is interpreted as normal when using WHO Z-score cut-off values for HAZ (Table 2.2).

The distribution of most other measurements, such as weight, skinfold thickness, etc. has an asymmetrical shape. The distribution in Figure 2.6 is asymmetrical to the right and described as right-skewed.

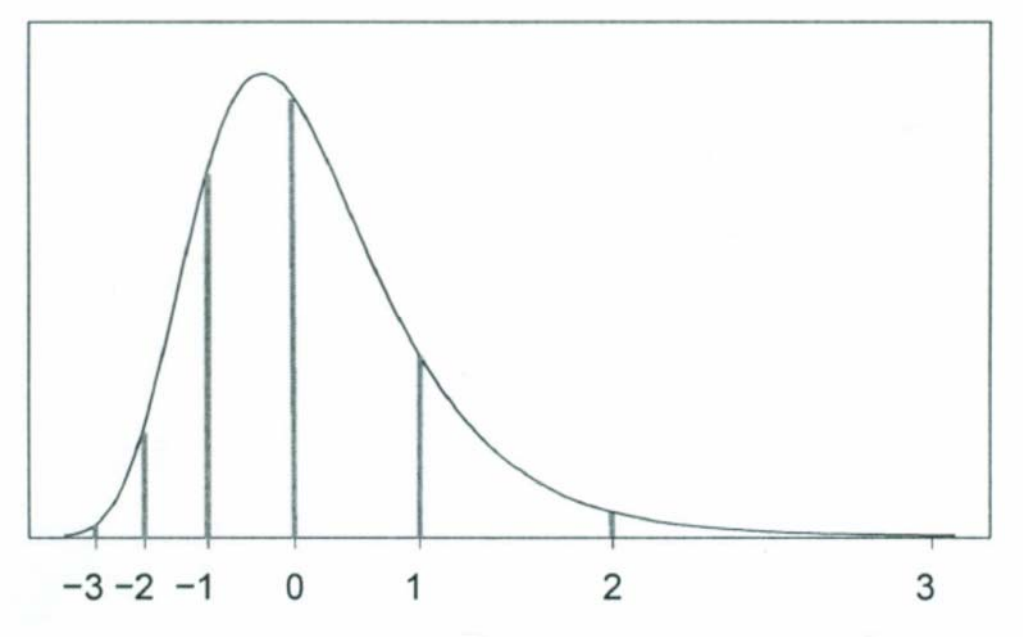


Figure 2.6 Right-skewed distribution curve cut into z-score segments (WHO, 2008:47)

The calculation of z-scores for measurements that are not normally distributed is more complicated than for that of normal distributions. In an asymmetrical distribution, distances between adjacent z-scores are not constant. For example, the distance between z-scores 3 and 2 is greater than between z-scores 2 and 1. Differences between the median and values at negative z-scores are smaller than the differences between the median and values at corresponding positive z-scores. However, percentages between the various z-scores are the same as in the normal distribution, namely 13.59% between -1 and -2, and 2.28% between -2 and infinity and +2 and infinity.

A series of mathematical calculations that take into account the asymmetrical distribution of measurements in the reference population is used to calculate the z-score of an observed point in an asymmetrical distribution. The formula used for this calculation is referred to as the lambda, mu, and sigma (LMS) formula (WHO, 2008:48):

$$\text{Z-score} = \frac{(\text{observed value} \div M)^{L} - 1}{L \times S}$$

The LMS formula is used to calculate z-scores for weight-for-age (WAZ), weight-for-length/height (WHZ), and BMI/A (BMIZ).

M, L and S are values for the reference population. M is the reference median value and estimates the population mean. L is the factor used to normalize the data (remove skewness, and S is the coefficient of variation (or equivalent).

For calculation of Z-score in a skewed distribution, the WAZ for the boy in the previous example is calculated. The boy has a weight of 11.9 kg at the age of 2 years and 4 months. To calculate a z-score for his weight-for-age, the M, L and S reference values for boys' weight at age 2 years and 4 months must be available. Those values are:

M = 12.94 (median weight for boys age 2 years and 4 months)
L = -0.06 (power to normalize the data)
S = 0.12 (coefficient of variation)

Using the formula, the z-score for weight-for-age for this boy is:

$$\frac{(11.9 \div 12.94)^{-0.06} - 1}{-0.06 \times 0.12} = -0.70$$

The boy's WAZ is below the median (0) but is still above -1.
Using the WHO cut-off values, the WAZ for the boy in the example is in the normal range (Table 2.2).

2.6.3.2 Percentiles

A percentile is a value on a scale of one to one-hundred that indicates the percentage of a distribution that is equal to or below it. Percentiles range from lowest to highest, with the average equal to 50 (or the 50th percentile). A percentile ranks the individual measurement relative to the other individuals used in the reference. For instance, if a child's height is

equal to the 15th percentile that means that the child's score is equivalent to that achieved by 15% of children of the same age. Likewise, if the child's height is equivalent to the 95th percentile of height, it implies that 95% of the population for his age and gender is smaller (Frisancho, 2008:304).

In a normal distribution percentiles and Z-scores are directly related. Table 2.3 gives the equivalents of percentiles and Z-scores in a normal distribution. E.g. a Z-score of -1.645 corresponds to an observation on the 5th percentile, just as a value at the 95th percentile will correspond to a Z-score of 1.645. Z-score values are commonly referred to as -3, -2 or -1 Z-scores. These Z-score values are equal to the 0.13th, 2.28th and 15.8th percentiles respectively (Gibson, 2005:338).

Table 2.3 Equivalents of percentile and Z-scores in a normal distribution (Gibson, 2005:338)

Below mean		**Above mean**	
Percentile	**Z-score**	**Percentile**	Z-score
5	-1.645	55	0.126
10	-1.282	60	0.253
15	-1.036	65	0.385
20	-0.842	70	0.524
25	-0.675	75	0.675
30	-0.524	80	0.842
35	-0.385	85	1.036
40	-0.253	90	1.282
45	-0.126	95	1.645
50	0.00		

The reference limits of below the 3rd or 5th percentiles, are commonly used to designate individuals as "at risk" for undernutrition or being undernourished, or above the 97th or 95th percentile as "at risk" for overweight or being overweight.

Percentile scores are available in table form as well as in chart form. Charts for W/A (referred to as Growth Charts or Road-to-health charts) are commonly used in clinical settings for routine monitoring of growth of individual children. Percentile charts for all other anthropometric measurements are also available, although not necessarily used

routinely. Percentile charts based on data from the different reference populations are available, e.g. NCHS percentile charts, CDC percentile charts and WHO percentile or Z-score charts. Figure 2.7 is an example of a CDC percentile chart of length-for-age (L/A) for girls from birth to age 36 months.

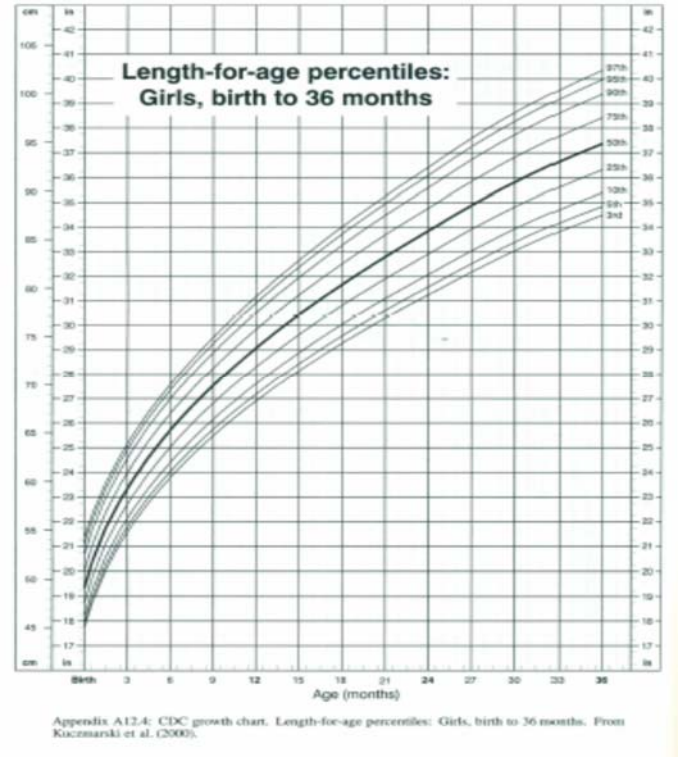


Figure 2.7 CDC Growth Chart: Length-for-age percentiles: Girls, birth to 36 months (Gibson, 2005:844)

Figures 2.8, 2.9 and 2.10 show WHO growth charts for W/A (Girls birth to 2 years), weight-for-length (W/L) (Girls birth to 2 years) and L/A (Girls 6 months to 2 years). In the WHO percentile charts, percentile values were replaced by Z-score values. The line labelled 0 represents the median, or average. The Z-score lines indicate distance from the average. The median and the z-score lines on the WHO charts were derived from measurements of children in the MGRS. Z-score lines on the growth charts are numbered positively (1, 2, 3) or negatively (-1, -2, -3), corresponding to Z-score distribution graphs. The general interpretation is that a plotted point that is far from the median in either direction, namely close to the 3 or -3 Z-score lines, may represent a growth problem. The points are read as follows:

- A point between the Z-score lines -2 and -3 is “below -2”

o A point between the Z-score lines 2 and 3 is “above 2” (WHO, 2008:13)

Figure 2.8: **WHO Weight-for-age chart for girls aged 6 months to 2 years (WHO, 2008:18)**

Figures 2.8, 2.9 and 2.10 illustrate how WHO percentile charts are used to evaluate a child’s anthropometric nutritional status. The example is of a girl aged 1 year 0 months, who is 67.8 cm long, and weighs 7.6 kg. Figure 2.8 shows her plotted W/A chart, Figure 2.9 is her W/L chart and Figure 2.10 is her L/A chart. The definitions in Table 2.1 are applied to evaluate the child’s plotted W/A, W/L and L/A in terms of Z-scores. In Figure 2.8 her plotted W/A is low, but still in the normal range. Her W/L is on the median (Figure 2.9), giving the impression that her growth is normal. In Figure 2.10 the plot position of her L/A is below the –2 Z-score line, showing that she is stunted.

Figure 2.9: **WHO weight-for-length chart for girls aged birth to 2 years (WHO, 2008:19)**

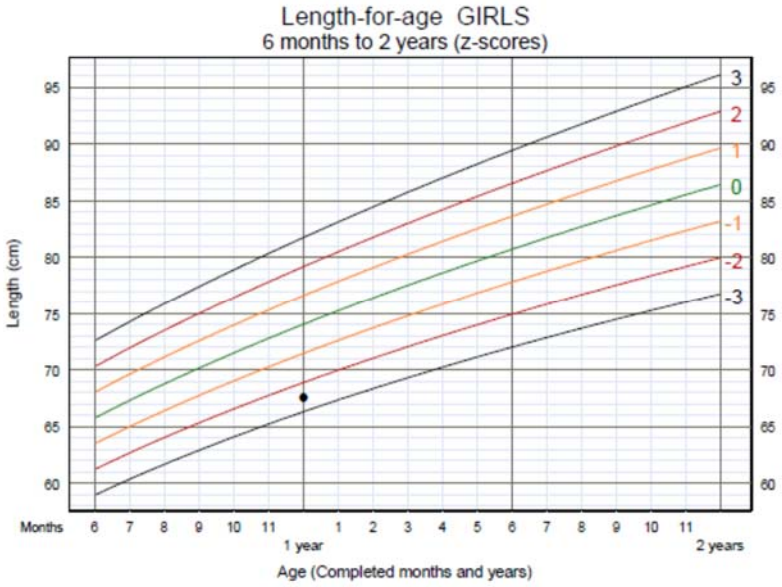


Figure 2.10: **WHO Length-for-age chart for girls aged 6 months to 2 years (WHO. 2008:19)**

The definitions included in Table 2.2 refer to the plot position on the chart, e.g. by being plotted above or below a particular Z-score line. If the plot position is exactly on the Z-score line, it is considered to be in the less severe category. For example, weight-for age on the -3 Z-score line is considered “underweight” and not “severely underweight” (WHO, 2008:13).

2.6.3.4 Percent-of-median

When it is not possible to calculate percentiles and Z-scores, the anthropometric measurements can be expressed in terms of percent-of-median. However, this provides only limited information on the relative position of the value in the reference population (Gibson, 2005:336).

Percent-of-median is expressed as the weight of the individual child relative to the average weight of the reference population children in the same age range, expressed as a percentage (London, 2009:Online). Percent-of-median can be calculated from anthropometric tables.

In the example, a girl who is 80 cm tall and weighs 8.0 kg will have a W/H percent-of-median of 78.4% according to the calculation below. The classification of anthropometric nutritional status according to the W/H percent-of-median is shown in Table 2.4 (London, 2009:Online).

In the anthropometric table for W/H of girls 24-59 months of age, the average weight for 80cm tall girls is 10.2kg. The percent-of-median for the 8.0 kg girl is thus calculated as 8.0 as a percentage of 10.2, or:

$$\frac{\text{Weight of subject (kg)}}{\text{Average weight of 80 cm tall girls (kg)}} \times 100 = \text{percentage of median}$$

$$= \frac{8.0}{10.2} \times 100 = 78.4\%$$

Table 2.4 Percent-of-median classification for weight-for-height (London, 2009:Online)

Weight-for-height percent	**Classification**
≥ 80%	Normal weight-for-height/normal anthropometric nutritional status
70 – 79%	Moderate acute protein-energy malnutrition
< 70%	Severe acute protein-energy malnutrition

The girl in the example has moderate acute protein-energy malnutrition, as defined by the 78.4% W/H percent-of-median value (London, 2009:Online).

W/H is not useful if a child has oedema. All children with bilateral oedema are automatically defined as having severe acute PEM regardless of their W/H percent-of-median value (London, 2009:Online).

Percent-of-median is especially useful when the distribution of the reference data has not been normalised, as is the case with the earlier Harvard reference data. This explains why so many of the first classification schemes based on the Harvard reference data (e.g. Gomez and Wellcome classification) used percent-of-median (Gorstein et al., 1994:273-283).

Percent-of-median does not provide the same information as the Z-score. The relationship between percent-of-median and the Z-score differs with age and height. An important limitation of percent-of-median is that the interpretation of specific percent-of-median varies across age groups and growth indices, which is not the case with Z-scores. This arises because the calculation of the percent-of-median does not take into account the distribution of the data within the reference set. The percent-of-median calculation also does not take into account the fact that the widths of the distributions of the W/A, W/H and H/A indices are not the same (Waterlow et al., 1977:489). Because of these variations, it is not possible to use a constant percentage of the reference median (e.g. 70%) across all ages and for all growth indices. For example, malnutrition at 60% of median W/A is much more severe in younger children than in older children. Moreover, 60% of the median for W/H cannot be used because such a deficit at any age is incompatible with life (Dibley et al., 1987:739).

In summary, each of the three anthropometric data-reporting systems has characteritics that need to be taken into consideration when deciding which system to use, as shown in Table 2.5.

Table 2.5 The characteristics of three anthropometric data-reporting systems (WHO, 1995:9).

Characteristic	Z-score	Percentile	Percentage of median
Adherence to reference distribution	Yes	Yes	No
Linear scale permitting summary statistics	Yes	No	Yes
Uniform criteria across all ages and indices	Yes	Yes	No
Useful for detecting changes at extremes of the distributions	Yes	No	Yes

2.7 MANAGEMENT OF HIV/AIDS

Management and treatment of HIV/AIDS should consist of a multidisciplinary approach. The three main approaches are the treatment of opportunistic infections through medical intervention, the use of ART, and suitable nutrition intervention.

2.7.1 Medical Intervention

Before the availability of ARV medications, medical intervention was the only option for HIV-infected patients. Medical intervention is aimed at the prevention or treatment of opportunistic infections in HIV-infected patients. Aggressive treatment of opportunistic infections is essential to prevent the deleterious effects of secondary disease from progressing and further weakening the patient.

Treatment decisions should be individualised according to the stage of disease progression in each individual patient. The goals of medical management of HIV should be to contain opportunistic infections in order to reduce HIV-related morbidity and mortality, improve the patient's quality of life, restore and preserve immunologic function, and suppress viral replication. Both medical and nutritional management should strive to optimise and extend the usefulness of currently available therapies, minimise drug toxicity and manage side effects (Fenton & Silverman, 2008:1001).

Diarrhoea is one of the most frequent symptoms of HIV and must be treated immediately, regardless of whether or not the cause is identified. Treatment of diarrhoea usually includes the use of a combination of antidiarrhoeal agents (Fenton & Silverman, 2000:899).

2.7.2 Antiretroviral treatment

2.7.2.1 Advantages of ART

ART suppresses progression of HIV-disease through several mechanisms, such as reducing concentrations of the virus in the infected person's blood by suppressing multiplication of the HI-virus. By keeping the viral load as low as possible, the damage to the immune system is controlled, HIV progression is contained and the onset of AIDS is delayed. Indications are that the growth impairment often seen in HIV-infected children can be prevented when ART is initiated at an early stage (Verweel *et al*., 2002:e23; Newell *et al*, 2003:e58, Musoke *et al*., 2010:56; Ramalho *et al*., 2011:454).

The development and wider availability of anti-retroviral medications have led to dramatic decreases in the number of deaths and new infections among adults and children living with HIV/AIDS in those countries where the medications are available (WHO, 2010a:1). The incidence of many of the opportunistic infections seen in HIV-infected persons has dropped dramatically, especially for pneumonia, wasting syndrome, Kaposi's sarcoma, *Mycobacterium avium* complex, CMV retinitis and cryptosporidiosis (Fenton & Silverman, 2008:1001).

2.7.2.2 When to initiate ART in children

Many obstacles, such as limited screening for HIV, a lack of affordable simple diagnostic testing technologies for HIV in young children and a lack of affordable practicable paediatric ARV medications are hindering implemention of ART in pediatric care, especially in developing countries (WHO, 2006a:Online). The WHO treatment regimes of 2006 for

introducing ART to infants and young children have been revised during 2010 in an effort to enhance access to ART for infants and young children (Table 2.6).

Table 2.6 WHO Recommendations for inititiating ART in infants and children; revised 2010 (WHO, 2010a:25)

AGE	Infants and children <24 months of age [a,b]	≥24 months of age to 59 months of age	Five years of age or older
%CD4+	All [c]	≤ 25	NA
Absolute CD4	All [c]	≤ 750 cells/mm^3	≤ 350 cells/mm^3 (As in adults)

a All HIV-infected infants should receive ART due to rapid rate of disease progression
b Countries with reliable access to CD4 monitoring may choose to apply clinical and immunological criteria for initiation of ART in children aged 12 – 23 months
c In children with absolute lymphopaenia, the CD4 percentage (%CD4+) may be falsely elevated

2.7.2.3 Special considerations related to ART usage

Despite the dramatic reduction in the number of HIV/AIDS death due to the introduction of ARV medications, ART has many risks and side effects, and therefore medication schedules must be followed strictly. Non-adherence can lead to drug resistance and development of resistant strains of the virus. On the other hand, side-effects from using the medications can make it difficult for a patient to adhere to the schedule. External factors also play a role in the ability of a patient to adhere to medication schedules (Bartlett, 2006:Online).

(i) Drug resistance

The activity of ARV medications and the effectiveness of treatment can be impaired by viral resistance. Without adequate blood level of active drugs, HIV mutates rapidly, causing resistance to the medications. High-level resistance to one medication can result in resistance to others of the same type. The development of resistance to at least one class of medication is seen frequently (Carpenter *et al*., 2000:381).

(ii) Adherence to medication schedules

Treatment regimens are usally complex, consisting of a combination of medications that have to be taken on different times of the day, some with food and others on an empty stomach.

Adherence of at least 95% to medication schedules is essential for ARV medications to be effective. Adherence to medication schedules ensures that the concentration of virus in the body is kept to a minimum and to minimise the development of viral mutations (Carpenter *et al*., 2000:388).

Multiple factors play a role in a patient's adherence to medication schedules, e.g. a busy work schedule, change in routine, running out of medications, having too many medications to take, side effects or not wanting other people to know that you are HIV-infected (Chesney *et al*., 2000:255,264). Side effects such as diarrhea, nausea, anorexia, severe headache, coughing, shortness of breath, thrush, and oral pain can all have an influence on a patient's adherence to medication schedules (Gifford *et al*., 2000:386). Many have suggested that these problems should be managed with informed health workers and patient education on the importance of treatment adherence (Musoke *et al*., 2010:56; Scherpbier *et al*., 2006:Online; Verweel *et al*., 2002:E25). A number of foods and supplements are known to alter the effects of antiretroviral drugs, providing many opportunities for food-drug interactions. It is also possible that some micronutrient deficiencies may make the drugs less effective, or may worsen side effects.

The South African government has recently rolled out a new single tablet to treat HIV/AIDS. This tablet is a combination of three tablets in one. Instead of taking three tablets a day, twice a day, HIV-infected patients now only have to take one small tablet once a day. The new tablet also has less side effects compared to other combined tablets. Another advantage is that this tablet costs more than a third less than the combination therapy that it will be replacing (Mungadze, 2013:Online).

Many patients often do not take the medication because it has to be taken with food. Nutrition and food security will have to be addressed when ARV medication is prescribed. From focus group discussions after the initiation of ART in Nairobi, most participants stated that lack of food is the most likely cause of non-adherence to drug therapy. The researchers Marston and De Cock (2004:79) commented as follows: "There truly is an irony, not captured in the language of treatment advocacy, in providing antiretroviral drugs to populations that lack access to safe water and food."

(iii) Side effects

Not all patients tolerate antiretroviral drugs. Life-threatening reactions include hepatic necrosis, Stevens-Johnson syndrome, lactic acidosis, and hypersensitivity. Serious reactions include pancreatitis, Fanconi syndrome (nephrotoxicity), renal calculi, marrow suppression, and transaminasemia. Milder reactions include gastrointestinal intolerance, peripheral neuropathy, rash, insulin resistance, hyperlipidemia, and fat atrophy or hypertrophy (Bartlett, 2006:Online).

There is evidence that malnourished people are less likely to benefit from antiretroviral treatment. Children who had recurrent opportunistic infections, severe anaemia, oral candidiasis and severe malnutrition have a high risk of mortality even when ART is administered. In at-risk children, careful timing of introduction of ART is essential to reap the benefits from ART (Callens et al., 2009:37). In resource-poor countries, treatment of children is made more difficult because many children with HIV are severely malnourished. Very little is known about how best to treat such children, and in particular whether it is best to start antiretroviral treatment before or after nutrition rehabilitation.

(iv) Importance of supportive care

Despite the successes with treatment with ARV medications, it is still of paramount importance that HIV/AIDS patients receive appropriate supportive care, including nutritional care. Attention should be given constantly to potential nutritional problems and their

consequences. Many studies have proven the importance of effective nutritional support to improve medical outcomes as well as the patient's quality of life.

2.7.3 Food based nutrition intervention

Nutrition intervention plays an important role in the prevention and treatment of HIV infection. For nutrition intervention to reach its goal, intervention should target the specific nutritional problems that are caused by the HIV infection, and should also address external factors such as inadequate access to food. A large number of food products for nutrition intervention are available, but the most suitable product should provide in the specific nutritional needs of the target group that it will be used for.

2.7.3.1 The role of food based nutrition intervention in HIV prevention and treatment

Poor nutritional status and increased nutritional vulnerability in HIV-infected children has been extensively documented. PEM is frequently seen in patients with advanced HIV disease, especially in the absence of ART (Fenton & Silverman, 2008:1008). Optimum nutrition to enhance nutritional status of HIV-infected children is essential in order to improve their quality of life (Knox *et al*., 2003:S66,67; WHO, 2006a:Online; World Bank, 2007:21; Kimani-Murage, 2011:12).

Although ARV medications have done a lot towards the reduction in HIV/AIDS mortality rates, it has become more and more clear that nutrition has an integral role to fulfil in HIV management, as well as in strategies for caring for HIV-positive individuals, affected households and communities (World Bank, 2007:3).

Food based nutrition supplementation plays an important role in the prevention of poor nutritional status and slowing down the progress of HIV disease, both in HIV-infected children receiving ART as well as in those not receiving ART (WHO, 2005:1,2). Nutrition supplementation is also important for the improvement of nutritional status in patients with already impaired nutritional status (Mason *et al*., 2004:558, Ivers *et al*., 2010:39, Fenton & Silverman, 2008:1010).

2.7.3.2 Goals of food based nutrition intervention

Food based nutrition supplementation for the treatment of HIV/AIDS should focus on prevention or treatment of PEM, prevention or treatment of micronutrient deficiencies, and management of HIV/AIDS related disorders. Risk factors such as inadequate access to food should also be addressed (ADA, 2000:711; Kimani-Murage, 2011:11).

The WHO Executive Committee has summarised a number of key findings and knowledge gaps regarding nutritional needs for HIV-infected adults and children, and used the information to compile feeding recommendations. The recommendation for energy intake for HIV-infected children is that energy intake should be increased at least 10% above the needs of uninfected children of the same age. If catch-up growth is needed, the energy intake should be even more – as much as 50% to 100% above that of uninfected children of the same age (WHO, 2003a:6; Krasovec *et al*., 2009:3). It is further recommended that these targets should be achieved through food-based approaches as far as possible (WHO, 2003a:6).

The quality of the diet is just as important as the quantity. High-energy, high-protein, nutrient-dense foods are recommended for HIV-infected children. Ten to 15% of total energy should be from protein (Krasovec *et al*., 2009:3). Fenton and Silverman (2000:904) recommend that a multi-vitamin supplement that provides 100% of the recommended dietary allowance (RDA) must be given, regardless of the dietary intake of the child.

2.7.3.3 Suitable products for food based nutrition intervention

Nutrition evaluation and suitable intervention should form part of the care package of all HIV-infected patients. Often the use of a supplement is needed to assist an HIV patient to consume the required amount of energy as well as macro- and micronutrients. The type of supplementation that will be suitable for a specific patient or group of patients should be selected with the specific nutritional needs and available resources in mind.

(i) Special requirements to consider for selection of food products

HIV-infected patients not only have to try to keep their normal body weight or often even have to regain lost weight, but they also have to put up with problems such as poor appetite, painful blisters in the mouth, malabsorption and anorexia. For them specifically it is important that a nutrition supplement should be more palatable and digestible, and should provide the maximum nutrition possible from the smallest volume possible (WHO, 2003a:66).

Depending on the stage of HIV infection and the presence of opportunistic infections, HIV-infected patients may at times feel too sick to prepare food. A supplement that is quick and easy to prepare can do a lot to ensure that the patient does not skip a meal because of a lack of time or energy to prepare the meal.

(ii) Types of products for food based nutrition intervention

A variety of supplements, ranging from foods that are ready for eating, to foods based on cultural staple foods and ready for reconstitution with a liquid before eating, are available for nutrition supplementation of HIV-infected patients. Due to the special needs of HIV-infected children in particular, a product that will be acceptable and affordable and provide in all the nutritional needs of the child will be the best option.

(a) Ready-to-use therapeutic food

Ready-to-use therapeutic food (RUTF) is an energy dense lipid rich paste made from peanut butter, milk powder, oil and sugar, with added vitamins and minerals. RTUF can be given as is, or it can be given in combination with habitual family foods. In a study by Ndekha *et al*. (2005:224), 56% of HIV-infected, severely malnourished Malawian children aged 12 – 60 months, who were given RUTF as part of home-based therapy after discharge from hospital, achieved complete anthropometric recovery. Two other groups of malnourished children in the same study received either RUTF supplement or maize-soy flour. Weight-for-height gain

as well as weight-for-age gain was more rapid in children receiving RUTF than in those receiving therapy with RUTF supplement or maize-soy flour. When compared to a group of children not infected with HIV, the results for non-infected children were even better. Recovery of HIV-infected children also took longer than for non-infected children. The HIV-infected children had more fever, cough and diarrhoea during their recovery time than the non-infected children (Ndekha *et al*., 2005:224).

An important advantage of the RUTF is the high energy and nutrient density of the food. The fact that it does not need any preparation before eating renders it very suitable for community-based treatment of severe malnutrition, where it has been found to give miraculous results, in the words of Stephen Moody, Senior Advisor for Food Technology, Office of Food for Peace. "As long as a severely malnourished child has enough appetite to consume them, the recuperative process will be complete in about six to ten weeks" (USAID, 2011:Online).

A possible disadvantage of RUTF is that it might cause more frequent diarrhoea than some other supplements. In a study of malnourished children of unknown HIV status that was run parallel to the above mentioned study, the children who received the maize-soy flour experienced significantly less diarrhoea than those on the RUTF (Manary *et al*., 2004:560).

(b) Enriched maize-soy instant porridge

Maize, which is the staple food of the majority of South Africans, is often used as basis to manufacture enriched, instant food supplements that just need the addition of a liquid (usually water) to be ready to eat. Soy protein is usually added to increase the protein value of the product. A variety of micronutrients are also added, usually to provide larger percentages of the RDA's of micronutrients for specific target groups.

These products have been used with success in home-based care nutrition supplementation programs in South Africa. However, it has some disadvantages especially for use in supplementation programs for young children. The main disadvantage is the low energy density when enough water is added to obtain a consistency that is suitable for a young

child. When less water is added to increase the energy density, the viscosity is too high for the feeding of a young child (Den Besten *et al*., 1998:4), because the volume the child has to consume to meet energy needs is too high for young children. The effect of feeding high-viscosity low-energy foods is even worse amongst ill, malnourished and anorectic HIV-infected children.

(c) Enriched, enzyme modified maize-soy instant porridge

The viscosity of starchy staple foods can be manipulated through the addition of the enzyme α-amylase. Amylase is an enzyme that hydrolyses starch and as a result reduces the viscosity of a starch-based food (e.g. maize porridge) to a level where the child can readily chew and swallow the porridge, thereby increasing the volume of porridge consumed. Amylase is added to food in the form of a flour manufactured from germinated grains (Den Besten *et al*., 1998:4; Chinnamma & Gopaldas, 1993). Various trials in feeding programs have shown that the addition of α-amylase to starchy, home-prepared staple foods does contribute to an increased energy intake by malnourished children (Gopaldas & Chinnamma, 1992:282; Chinnamma & Gopaldas, 1993:21; Den Besten *et al*., 1998:4).

Due to the problems of energy density explained in (b), and the advantages of adding α-amylase to home-made porridge, a manufacturer of enriched maize-based food supplements have added α-amylase to one of their enriched maize-based food supplements to enable young children to consume sufficient amounts of the product. The product is developed to provide in the specific nutritional needs of HIV-infected children in the age group six months to 10 years. The product has not yet been tested for its efficacy for HIV-infected young children.

The product is identical to the original enriched maize-based food supplement, except for the following(Table 2.7):

- α-amylase added to the product for HIV-infected children,
- Increased vitamin C in the amylase-product, to act as enhancer to improve mineral bioavailability
- sulphur added as preservative to the product for HIV-infected children

Table 2.7 Nutritional analysis per 100g of enriched maize-based porridge with and without added α-amylase (SABS analysis)

Nutrient	Product with added α-amylase	Product without α-amylase
Protein (g)	14.0	14.0
Total Carbohydrate (g)	61.2	61.2
Fat (g)	14.8	14.8
Energy (kJ)	1765	1765
Isoflavones (mg)	94	94
Vitamin A (µg RE)	600	600
Beta carotene (mg)	0.6	0.6
Vitamin D (µg)	15	15
Vitamin E (mg)	6	6
Vitamin C (mg)	**200**	**67.5**
Thiamine (mg)	1.2	1.2
Riboflavin (mg)	1.1	1.1
Niacin (mg)	11	11
Vitamin B6 (mg)	1.6	1.6
Folic acid (µg)	200	200
Vitamin B 12 (µg)	2.5	2.5
Biotin (µg)	50	50
Pantothenic acid (mg)	4	4
Vitamin K (µg)	30	30
Sulfur (mg)	**100**	-
Calcium (mg)	825	825
Phosphorus (mg)	660	660
Potassium (mg)	550	550
Iron (mg)	12.2	12.2
Magnesium (mg)	250	250
Zinc (mg)	15	15
Iodine (µg)	90	90
Manganese (mg)	1.8	1.8
Copper (mg)	1.8	1.8
Sodium (mg)	320	320
Molybdenum (µg)	25	25
Chromium (µg)	25	25
Selenium (µg)	40	40
Chloride (mg)	500	500

2.7.4 Overview of nutrition intervention in South Africa

Standard guidelines based on clinical studies can help the clinician/dietician in developing an appropriate and graded nutrition intervention strategy for any specific patient (Oleske *et al.*, 1996:2617S).

In South Africa nutrition intervention given by the Department of Health is guided by national guidelines, but provinces have to adjust quantities of supplements according to available budgets for nutrition intervention programs. For the last 10 years already almost all provinces have experienced that the budget is never sufficient to provide the "ideal" nutrition supplementation package for each HIV-infected patient. Especially some provinces (of which the Free State Province is one) had to cut on quantities extremely in order to provide at least part of the daily requirements to HIV-infected patients in need. This increased the need for a product that will provide maximum supplementation and will have maximum impact with regard to intake, digestion and absorption.

Targeted food supplementation for malnourished children and underweight pregnant- and lactating women was implemented by the South African Government more than 30 years ago. The type of food supplements used in this program is revised from time to time and changes to regimes are made when necessary. These changes are based on what suppliers have to offer as well as affordability and ease of distribution and re-constitution. With HIV/AIDS awareness underweight HIV/AIDS patients were added to the target groups for this program, and the nutritional needs of these patients are now also taken into consideration when a nutritional regime is revised.

Food mixtures that have been used over the years as nutrition supplements for malnourished children and underweight pregnant- and lactating women include vitamin-mineral-energy enriched instant maize products, high energy drinks, several instant porridges available in retail, food mixtures containing a maize product (e.g. samp) as base and a variety of other grains and legumes added to it, for use as a complete meal or as an ingredient in soups.

2.8 SUMMARY

Children are infected with HIV mostly through MTCT. The disease in children is much more aggressive with significantly faster progression compared to adults, leading to high mortality rates in young children. Suitable, timeous intervention can, however, slow down

progression of the disease and lead to longer life expectancy and improved quality of life for HIV-infected children.

Nutritional status and malnutrition in HIV-infected persons are closely related. The impact of HIV infection on the nutritional status of children, and the vicious cycle of malnutrition and disease underlines the importance of early prevention of both opportunistic infections and malnutrition in HIV-infected children. The development of malnutrition in HIV-infected children is influenced by several factors. The food intake of the HIV-infected person is often sub-minimum, due to symptoms of the infection and often also due to poor socio-economic conditions. The additional relative high nutritional needs of children, combined with negative influences on food intake, lead to even worse impairment of nutritional status.

Anthropometric measurements can be used to evaluate the nutritional status of children to determine the need for nutrition intervention. The same measurements can also be used to evaluate outcomes of treatment and intervention programs that target malnutrition. Medical intervention of HIV infection has as its goal to treat especially opportunistic infections and symptoms. ART has become much more freely available to HIV-infected persons and can prevent the virus from multiplying, whereby the progression of disease is slowed down and the life expectancy of the patient can be increased. However, nutrition intervention or nutrition therapy still remains one of the most important components of treatment of HIV-infected persons.

Despite ample data demonstrating the link between macro- and micronutrient deficiencies and poorer outcome for HIV-infected children, very little data regarding the outcome of nutrition intervention in HIV-infected patients is available, especially in relation to prospective studies in developing countries.

In a country where the majority of people live in poverty and lack the resources to provide in the increased needs of caring for one or more persons with HIV/AIDS, nutrition supplementation programs are essential to establish good nutritional status or correct poor nutritional status. However, although a large variety of supplements are available for this use, not many scientific studies have been carried out to compare the impact of

nutrition supplements on the anthropometric nutritional status of HIV-infected children. It is also important to remind the reader that HIV research is complicated from an ethics point of view. Yet, in South Africa, the need exists for a concentrated, energy-dense food that is culturally acceptable and that will provide in as much as possible of the energy and nutrient needs of HIV patients of all age groups. The need therefore exists for research in the development of new nutritional products. Products should be easy to prepare, either by a caretaker (often without any food preparation skills) or by a person who does not have the necessary physical energy to cook a full meal. Products should also be affordable, have a relatively long shelf life and be packaged in such a way that transport and distribution to patients is as easy and simple as possible without any risk of harmful bacterial contamination.

CHAPTER 3 - METHODOLOGY

3.1 INTRODUCTION

The aim of this study was to determine the impact of an enzyme modified, enriched maize based supplement on the anthropometric nutritional status of HIV-infected children in care centres in Mangaung. The impact of an enzyme modified nutrition supplement was compared to the impact of a supplement similar in nutritional value but without enzyme modification, on the anthropometric nutritional status of young HIV-infected children in child care centres.

The study design, study population, ethical considerations, variables, measuring techniques, pilot study, validity and reliability, study procedures, and statistical analysis of the data, as well as the problems encountered are described in this chapter.

3.2 STUDY DESIGN

This study formed part of a larger study in which four researchers participated. The layout of the different roles of the four researchers in the study is discussed in Table 3.1. The broader study was carried out to evaluate the impact of an enzyme-modified enriched maize supplement on the growth, immune and health status of HIV-infected children.

The researcher (Researcher 2) of the study reported in this document was responsible for the anthropometric measurements of the children and consequent evaluation of the impact of the supplementation on the anthropometric nutritional status, with special emphasis on growth, of the children.

The study design was that of a double-blinded, clinical, controlled randomised intervention trial. Children from the only six available care centres in Mangaung for the care of HIV-infected children were randomly selected for inclusion into either the experimental or the control group.

Table 3.1: Layout of different roles of the four researchers involved in the study

Researcher 1	**Researcher 2**	**Researcher 3**	**Researcher 4**
Development and coordination of total study design, development of the experimental product, evaluation of immune status, disease progression and biochemical parameters of nutritional status of study population before and after intervention	Collection and interpretation of anthropometric nutritional status data before, during and after intervention	Measurement of supplement consumption and energy intake of study population during intervention	Evaluation and monitoring of health status of study population before, during and after intervention

3.3 STUDY POPULATION

The study population consisted of anti-retroviral naïve, food secure HIV-infected children in the age group 12 months to 10 years. The children were cared for in the only six care centres in the Mangaung area of Bloemfontein that indicated that they took care of children infected with HIV (Table 3.2). For this specific group of institutionalised children, no specific recommendations or guidelines regarding nutrition support could be found.

Table 3.2: HIV in children screened with ELISA in six care centres in Mangaung

Name of centre	**Children tested (ELISA)**	**Children HIV-infected**
Centres with permanent residence:		
Lebone House Care Centre	70*	20*
Sunflower House Care Centre	15	5
Day Care Centres:		
Sunflower-, Bana Pele-, Bophelo- and Joan Marsden Day Care	70	12
Total for 6 centres	**155**	**37**

* One child in this group was younger than 18 months (13 months at baseline) and born to an HIV-infected mother. Due to the possibility of a false positive ELISA, only CD4+ count was done to confirm HIV infection.

3.3.1 Target Population

A total of six care centres that indicated that they focus on the care and support of HIV-infected children, were the target centres for the selection of the study children. These centres included two centres where children found permanent residence (they only went home or on visits to family over weekends and school holidays), namely Lebone House Care Centre and Sunflower House Care Centre, and four day care centres, namely Sunflower Day Care Centre, Bana Pele Day Care Centre, Bophelo Day Care Centre and Joan Marsden Day Care Centre. The four day care centres were all managed by Sunflower House Care Centre.

The inclusion of these care centres had several benefits for the study. One of the major benefits of using children in care centres was that food insecurity could be excluded as a possible cause of malnutrition, as the children had access to regular meals during the week. It was also believed that the study would have fewer drop-outs because the children were registered to attend these centres and were believed to be present during the time period of the study, and that the children would be more accessible for regular health screenings. Providing the children with supplements at the care centre, could also eliminate the possibility of misuse of the supplements by other family members.

3.3.2 Screening

Care centres in the Mangaung area were contacted to find out whether they took in children infected by HIV. Six of the care centres confirmed that they specifically took care of HIV-infected children. These six care centres were selected as the target care centres. The administrators of the care centres were then requested to give written consent for the planned study at these centres (Addendum A).

Meetings were arranged with the parents and legal guardians of the children (aged 12 months to 10 years) in the care centres. Informed consent (Addendum B) was obtained for the following two possible scenarios:

- Parents or legal guardians of children aged 18 months to 10 years were requested to give informed consent for enzyme-linked immunosorbent assay (ELISA) tests on their children, with possible inclusion of the child in the study if the ELISA test result was positive.
- Parents or legal guardians of children between 12 and 18 months, where the mother/father or guardians were willing to reveal the mother's positive HIV status, were requested to give informed consent to do a CD4+ count on the child, for possible inclusion of the child in the study.

ELISA tests cannot be used to differentiate between antibodies transferred across the placenta (of an HIV-infected mother) and those antibodies produced by the baby's immune system. Antibodies transferred across the placenta will imply HIV exposure. Antibodies produced by the baby's own immune system will imply HIV infection through MTCT. All babies born to HIV-infected women will have positive ELISA tests at birth. If the antibodies are due to HIV exposure, the antibodies will gradually disappear and by the age of 18 months the ELISA test result should be negative. This phenomenon is referred to as seroreversion. A child infected with HIV through MTCT, will not serorevert (Stevens and Sherman, 2009:Online). The ELISA test can thus give a false positive result in babies born to HIV-infected mothers if the test is performed before seroreversion could take place, in other words before the child is 18 months old.

The number of children for whom informed consent was received for testing with ELISA, and the number of children with positive ELISA, is shown in Table 3.2. A total of 154 children, of whom 69 (plus 1 child aged 13-months) were cared for in Lebone House Care Centre, 15 in Sunflower House Care Centre and 70 in the five day care centres (see Table 3.2) were screened with ELISA. From the total number of 154 children screened with ELISA plus the 1 13-month old child, only 37 had positive ELISA test results. The 37 children with positive ELISA were included in the study for baseline data selection.

3.3.3 Sample selection and sample size

After the initial screening of 154 children with ELISA, viral load tests were conducted on 37 children as set out in Table 3.2. The 37 children included 36 with positive ELISA + 1 child younger than 18 months and born to an HIV-infected mother. The viral load count served as confirmation of the diagnosis and for selection to the study group. For the final selection the following inclusion- and exclusion criteria were used:

3.3.3.1 Inclusion criteria

- HIV-infected children in centres as described in Table 3.2.
- Children 18 months to 10 years with a positive ELISA and HIV infection confirmed with CD4+ count.
- Children 12 to 18 months, born to an HIV-infected mother, and HIV infection confirmed with CD4+ count after obtaining consent from the parent or legal guardian.

3.3.3.2 Exclusion criteria

- HIV negative children
- Children not up to date with the immunisation programme
- Children with known allergies for soy
- Children with foetal alcohol syndrome or other chronic illness
- Children referred for ARV treatment
- Children without consent from the parent or legal guardian
- Children with advanced HIV disease

After screening as described (3.3.2), and application of the inclusion- and exclusion criteria (3.3.3), the sample size was 37 children. The initial plan was to include 70 HIV-infected children in the study. It was believed that the planned number of study children would be easy to obtain, since all the care centres earmarked for the study indicated that they focused on children infected with HIV. However, the results of the screening process with

ELISA showed that the majority of children cared for in these centres were affected by HIV/AIDS and not necessarily infected as assumed before the start of the project.

3.3.4 Stratification and randomisation

After inclusion in the study, baseline data of anthropometric nutritional status, immune status, biochemistry and health status were collected for the 37 study group children. The sample was then stratified according to gender and age of the children, anthropometric nutritional status (weight-for-age Z-score [WAZ]), CD4+ count and/or CD4 percentage, presence of TB, and whether the child was in a centre with permanent residence or in a day care centre.

A WAZ of less than minus two standard deviations (<-2SD) of the median from the NCHS or more than -2SD was used to differentiate between underweight and normal weight children. The level of immunosuppression was determined using the CDC 1994 classification system (Table 2.2, Chapter 2; WHO, 2008:14).

The stratification information was used to randomly place the children into two groups, an experimental (E) and a control (C) group. The stratification process ensured that each group represented children with similar characteristics in terms of gender, age, WAZ, CD4+ count and/or CD4 percentage, presence of TB, and place of residence. The stratification and randomisation into the E-group or the C-groups were done by the Department of Biostatistics, Faculty of Health Sciences, University of the Free State. Through this process, 19 children were included in the E-group and 18 in the C-group. The diet of the children in the E-group was to be supplemented with the experimental product, and the C-group with the control product.

The researchers for this study were blind to the randomisation process as well as for the selection of the supplements. Only the manufacturer of the supplements knew which of the two products contained the enzyme mixture. To ensure that children in both the E- and C-groups received the correct supplements respectively, colour coding was used. The experimental and control products were packed in plastic bags with two different colours,

mixed in bowls of which the colours matched the packaging colours, and dished up in cups or bowls of the same colours as the packaging and mixing bowls. Only after completion of the intervention the researchers were informed as to which colour represented which group.

3.3.5 Drop-outs

During the course of the study, children who refused to eat the supplements as well as drop-outs were recorded and documented.

Only 29 of the 37 children who were initially included in the study, completed the intervention. Eight children did not complete the intervention or were removed from the study group due to a number of different reasons. The reasons for dropping out or not completing the intervention are summarised in Table 3.3.

Table 3.3: Summary of number of drop-outs and reasons for dropping out

Reason for dropping out	**Number of children**
Deceased	2
Hospitalised	1
Continued refusal to eat the supplement	1
Chronic diarrhoea	2
Adopted	1
Intermittent day care visits	1

3.4 ETHICAL CONSIDERATIONS

Ethical approval was obtained from the Ethics Committee of the Faculty of Health Sciences (ETOVS no. 190/00C). Approval was obtained from the Head Administrators of each of the care centres included in the study to conduct the study at these facilities. Approval was obtained in writing from each of the Head Administrators of the centres. Addenda A1 and A2 are examples of the letters of approval that were signed by the Head Administrators of the two main care centres, Lebone House Care Centre and Sunflower House Care Centre. The head administrator of Sunflower House Care Centre signed on behalf of the four day

care centres, which are all functioning under the supervision of Sunflower House Care Centre.

The information on the informed consent form was explained in the home language of the mother or legal guardian, and the form was signed by two witnesses. All mothers, or legal guardians in the case of orphans, gave written, informed consent for the initial HIV testing and received free counselling before and after the test. All mothers and guardians of HIV-infected children, who agreed that their children could participate in the intervention, signed consent forms (Addendum B). The consent forms were available in Afrikaans, English and Sesotho.

Only names and record numbers were used on all forms for data capturing, no reference was made to personal information of the participants (Addendum C, D, F, G, H).

The control product that was consumed by the C-group, and the test product that was consumed by the E-group, were similar with regard to nutritional value. Both groups received exactly the same nutritional benefit. The only difference between the two products was that the test product contained added α-amylase, which was intended to decrease the viscosity of the reconstituted product. The children in the E- and C-groups also received the same amounts of supplement to ensure that no participant in the study was affected negatively.

The ethical principal was applied that, if the outcome of the study indicated that children in any of the groups experienced significant improvements in growth, immune, micronutrient and health status, the supplements would have to be provided to them free of charge for as long as they benefit from it.

3.5 VARIABLES AND OPERATIONAL DEFINITIONS

The variables that were measured for the purpose of this study included anthropometric measurements in three main categories, namely weight/height status, head circumference and upper arm anthropometry.

3.5.1 Weight-height-status

Weight/height status of children were expressed as W/A, H/A, and BMI/A Z-scores (SD) and evaluated according to the WHO Growth Standards (Frisancho, 2008:CD-ROM) and WHO Z-score cut-off values (WHO, 2008:14; 2009b:10) (Table 3.4). The W/A, H/A, and BMI/A Z-scores (SD) were also evaluated according to the CDC 2000 Growth Reference Values (Frisancho, 2008:CD-ROM) and the Z-score cut-off values of the NCHS/CDC (Lee & Nieman, 2010:169, Table 6.1) (Table 3.4).

Table 3.4 Categories for weight/height status in children according to WHO Z-score (SD) cut-off values (WHO, 2008:14; 2009b:10)

Z-score (SD)	HAZ	WHZ	WAZ	BMIZ
> 3 SD	Above normal	Obese	Possible growth problem	Obese
> 2 to ≤ 3 SD	Normal height	Overweight	Possible growth problem	Overweight
> 1 to ≤ 2 SD	Normal height	Possible risk of overweight	Possible growth problem	Possible risk of overweight
< 1 to 0 to ≥-1	Normal height	Normal weight	Normal weight	Normal weight
<-1 to ≥-2 SD	Normal height	Normal weight	Normal weight	Normal weight
<-2 to ≥ -3 SD	Stunted	Wasted	Underweight	Wasted
> -3 SD	Severely stunted	Severely wasted	Severely underweight	Severely wasted

Table 3.5 Categories for weight-height status in children, according to NCHS/CDC Z-score cut-off values (Lee & Nieman, 2010:169, Table 6.1)

Z-score	HAZ	WHZ	WAZ	BMIZ
> 2 SD	Above normal	Overweight	Overweight	Overweight
≤ 2 to > -1 SD	Normal height	Normal weight	Normal weight	Normal weight
≤-1 to > -2 SD	Mildly stunted	Mildly wasted	Mildly underweight	Normal weight
≥-2 to ≤-3 SD	Moderately stunted	Moderately wasted	Moderately underweight	Underweight
< -3 SD	Severely stunted	Severely wasted	Severely underweight	Severely underweight

3.5.2 Head circumference

HC of children was expressed as HC-for-age (HC/A) percentile values and evaluated according to the WHO Growth Standards (Frisancho, 2008:CD-ROM) and percentile cut-off

values for anthropometric nutritional status shown in Table 3.6 (Frisancho, 2008:306, 314). HC was evaluated for the age group 12 to 72 months, which is the maximum age for which HC/A can be evaluated using the WHO Growth Standards (Frisancho, 2008:CD-ROMb).

Table 3.6 Categories for head circumference-for-age in children according to percentile cut-off values for the evaluation of anthropometric nutritional status (Frisancho, 2008:306, 314)

Percentile	**Classification**
<5	Small head circumference
≥ 5 to ≤ 14.9	Below average head circumference
≥15 to ≤ 84.9	Healthy range of head circumference
≥ 85 to ≤ 94.9	Above average head circumference
≥ 95	Large head circumference

3.5.3 Upper arm anthropometry

Upper arm anthropometry refers to MUAC and TSF measurements, from which UAMA and UAFA were calculated. MUAC, TSF, UAMA and UAFA were expressed as the measurement for age, namely MUAC/A, TSF/A, UAMA/A and UAFA/A and were evaluated according to the Comprehensive Anthropometric Reference based on the NHANES III for children and adults (Frisancho, 2008:VII, 112, CD-ROM) and the percentile cut-off values for anthropometric nutritional status (Frisancho, 2008:306, 314-317) shown in Table 3.7

Table 3.7 Categories for MUAC/A, TSF/A, UAMA/A and UAFA/A in children according to percentile cut-off values for the evaluation of anthropometric nutritional status (Frisancho, 2008:306, 314-317)

Percentile	**MUAC**	**TSF**	**UAMA**	**UAFA**
<5	Low	Lean	Low muscle, wasted	Low fat mass, wasted
≥ 5 to ≤ 14.9	Below average	Below average	Below average	Below average
≥15 to ≤ 84.9	Healthy range	Healthy range	Healthy range	Healthy range
≥ 85 to ≤ 94.9	Above average	Above average	Above average	Above average
≥ 95	Excessive	Excess fat	High muscle, good nutrition	High fat mass

3.6 MEASURING TECHNIQUES

All anthropometric measurements were taken by a trained field worker (Researcher 2). Standardised techniques as described by Frisancho (1990:10-19), were used throughout the study period to esure accurate and standardised measurements.

3.6.1 Weight

A SECA electronic scale (model 708) was used to weigh children over two years of age and who could stand on their own. The scale was calibrated monthly by using objects of known weight. Before weighing children, the scale was placed on a flat, hard surface. Children were weighed without shoes in only light clothing and had to stand independently in the middle of the platform with the body weight evenly distributed on both feet. The weight measurement was taken once with every weighing session, once the measurement on the scale signalled as stabilised. The weight of children was recorded to the nearest 0.01 kg.

Babies and children younger than two years who could not stand on their own were weighed on a baby scale with a levelled pan to support the baby. The scale was calibrated before every weighing session using objects of known weight. Babies were weighed without diapers, and with heavy clothing removed. When putting the baby on the scale, care was

taken to have the weight distributed equally on each side of the centre of the pan. Weight was recorded to the nearest 50 g. Measurements of weight were done at weekly intervals for the duration of the study. Weights were recorded on a form for weekly weight measurements, designed for this study (Addendum C). Every fourth week the weight was recorded together with other anthropometric measurements, on a form for four-weekly measurements (Addendum D).

3.7.2 Height or length

The height of children older than two years of age who could stand on their own was measured with a calibrated stadiometer. The stadiometer consists of a metric tape affixed to the vertical arm of the device. The stadiometer has another arm that slides inside the bottom arm, the top arm having a 90 degree horizontal fixture that is brought down to the crown of the head.

Children were measured without shoes. Children were instructed to stand with heels together and back as straight as possible; the heels, buttocks, shoulders and head touching the vertical back bar of the device. The weight of the child was to be evenly distributed on both feet and the head positioned in the Frankfort horizontal plane. The child's arms were hanging freely at the sides with the palms facing the thighs. The children were asked to inhale deeply and maintain a fully erect position. The movable horizontal bar is brought down until it touches the head; making sure to put sufficient pressure to compress the hair. Where needed, braids were loosened to ensure correct measurement. The measurement was recorded to the nearest 0.1 cm. Only one measurement per session was taken for each subject.

The length of children under two years of age was taken in the recumbent position. An infantometer (Pedobaby Babymeter) with calibrated, non-stretchable tape measure was used. The measuring tape fixed to the infantometer was marked off in millimetres with the zero at the edge of the headboard. Infant length was recorded as the distance between the headboard and the footboard. Two people (the examiner and an assistant) were doing these measurements together to ensure accuracy. An assistant was standing at the head of the

table, holding the infant's head against the headboard. The examiner straightened the infant's legs holding the feet with toes pointed directly up, and moves the footboard against the feet. The measurement is indicated by the position of the footboard and is recorded to the nearest 0.1 cm. Only one measurement per session was taken for each subject.

Measurements of height were done at 4-weekly intervals during the duration of the study, and recorded on a form for 4-weekly anthropometric measurements, designed for this study (Addendum D).

3.6.3 Head circumference

A non-stretchable tape was used to take the HC measurement. Before taking the measurements, all hair ornaments and braids were removed. The measurement was taken by placing the tape across the frontal bones just above the eyebrows, around the head above the ears on each side, over the occipital prominence at the back of the head, and was moved up and down over the back of the head to locate the maximal circumference of the head. The tape measure was held perpendicular to the long axis of the face and pulled firmly to compress the hair and underlying soft tissues. Children who were calm were standing while the measurement was taken. Children who could not stand or sit on their own, were held on the lap of an assistant while the measurements were taken. Measurements were recorded to the nearest 0.1 cm.

Measurements of HC were done at four-weekly intervals during the duration of the study, and recorded on a form for four-weekly anthropometric measurements, designed for this study (Addendum D).

3.6.4 Mid-upper arm circumference

The measurement of MUAC was taken with a non-stretchable metric tape. The child was requested to keep the right arm bent at the elbow at a 90-degree angle, with the upper arm held parallel to the side of the body. A tape was used to measure the distance between the acromion and the olecranon process of the elbow. The midpoint between the two marks

was marked with a soft pen. Then the child was requested to let the right arm hang loose at his or her side. The metric tape was positioned around the upper arm at the previously marked midpoint. The tape was held snug, but not so tight as to cause skin indentation or pinching. The circumference was recorded to the nearest mm.

Measurements of MUAC were done at four-weekly intervals during the duration of the study, and recorded on a form for four-weekly anthropometric measurements, designed for this study (Addendum D).

3.6.5 Triceps skinfold thickness

TSF thickness was measured with a calibrated Harpenden skinfold caliper. TSF was measured at the marked midpoint (described in 3.6.4) of the posterior of the right upper arm. The child was standing with the right arm hanging loosely by his/her side. The examiner grasps a vertical pinch of skin and subcutaneous fat between the thumb and forefinger about 1 cm above the previously marked midpoint, gently pulling the skinfold away from the underlying muscle. The jaws of the skinfold caliper is placed on the skinfold at the marked midpoint, perpendicular to the length of the fold, while maintaining a gentle grasp on the skinfold. Three readings were taken in quick succession, while the fingers continued holding the skinfold. The reading was taken from the skinfold caliper as soon as the jaws of the caliper came into contact with the skin and the dial reading was stabilised. Readings were recorded to the nearest 0.1 mm and all three the readings were recorded. The average of the three readings was used in interpretations and for calculations.

Measurements of TSF were done at four-weekly intervals during the duration of the study, and recorded on a form for four-weekly anthropometric measurements, designed for this study (Addendum D).

3.6.6 Upper arm muscle area

Measurements of the MUAC and TSF were used to calculate the UAMA. The UAMA is an estimation of the area of the bone and muscle portions of the upper arm (Frisancho 2008:314).

The calculations were done using the following formulas (Frisancho, 1990:20):

$TUA = (C^2)/(4 \times л)$

$UAMA = \{C - TSF \times л)^2/(4 \times л)$

(C = circumference of the upper arm, TSF = triceps skinfold thickness, TUA = total upper arm area)

3.6.7 Upper arm fat area

Measurements of the MUAC and TSF were used to calculate the UAFA. UAFA is an estimation of the area of the fat portions of the upper arm (Frisancho 1990:21). UAFA is calculated using the following formula (Frisancho 1990:21):

$UAFA = (TUA - UAMA)$

3.8 TRAINING OF FIELD WORKERS

Researcher 3 was responsible for training the staff at the different centres to prepare and serve the food according to the research protocol. For this, Researcher 3 developed a standardised training manual (Addendum E) which explained the measuring, mixing and serving procedures. The training manual also included basic nutrition knowledge and information on food hygiene, which would not only be to the benefit of the study children but also to the care centres involved.

Researcher 2, who would be responsible for taking the anthropometric measurements, underwent training and standardisation of techniques with the assistance of a level 2 kinanthropometrist.

3.8 PILOT STUDY

Before the start of the main study, a pilot study was carried out with 11 children at Oraratile Adra Care Centre in Mangaung for a period of four days. Oraratile Adra Care Centre was selected for the pilot study because it is also a centre caring for children affected by or infected with HIV. Oraratile Adra Care Centre could not be considered for the intervention study because another nutrition intervention project was due to start at the centre within the same time period as the planned study.

The aim of the pilot study was to test the acceptability and ease of use of the experimental and control supplements, the measuring techniques of all the researchers, and the documentation of the data by all the researchers.

Researcher 2 used the pilot study to check the accuracy and standardisation of the researcher's anthropometric measuring techniques and the suitability and ease of use of the forms for the capturing of anthropometric data. Researcher 3 used the pilot study to test the suitability and usefulness of the training manuals (Addendum E, compiled by Researcher 3) for training of the care centre staff that would be responsible for the reconstitution and serving of the supplements to the study children in the care centres.

After completion of the pilot study, final changes were made to forms, questionnaires and the training manuals by the researchers where necessary.

The pilot study was also used to get an indication of the amounts of the two products the children would consume. Children were given 150 g (dry weight) or 450 g (reconstituted) of the experimental product for two days and were then fed the same quantities of the control product for two days. Leftovers were weighed on an electronic scale. None of the children in the pilot study refused either of the supplements, indicating that both supplements were acceptable and could be used in the study.

3.9 VALIDITY AND RELIABILITY

Validity determines whether the research truly measures that which it was intended to measure, and how truthful the research results are (Block & Hartman, 1989:1133; Joppe, 2000:Online).

To ensure validity of anthropometric measurements, scales and other anthropometric equipment were calibrated before the start of the study. Scales were checked and calibrated on a weekly basis during the duration of the study, and other anthropometric equipment was checked monthly during the study period. Other researchers played a key role in determining the exact quantities of experimental and control product the children consumed. The current researcher (Researcher 2) in collaboration with the other researchers did regular checks to ensure that the study children in the E-group continued to receive the E-product, and those in the C-group the C-product.

Reliability refers to the ability of a method to produce the same estimate on more than one occasion, assuming that nothing has changed between the two occasions (Block & Hartman, 1989:1133). For a study to be reliable, the results have to be consistent over time, the study procedures and methods should be such that it can be reproduced, and the study should be an accurate representation of the total population under study (Joppe, 2000:Online).

To ensure reliability of anthropometric measurements, the researcher was trained and standardised by a level 2 kinanthropometrist before the study. The trained researcher (Researcher 2) took all the anthropometric measurements of all the study children for the full duration of the study. To ensure that the correct type and amount of supplement is fed to each child, Researcher 3 measured the correct amounts of each of the Experimental and Control products for each child for every day into individually marked sachets. Researcher 3 trained the kitchen staff of those facilities included in the study the correct method to reconstitute the supplement and to also ensure that each child receives the supplement according to the group into which the child was selected.

3.10 STUDY PROCEDURES

The study was carried out in four phases, namely the initial phase, baseline data collection, intervention, monitoring and control, and end data collection. The procedures that were followed are summarised in the flow diagram in Figure 3.1.

3.10.1 Phase 1: Initial phase

All four researchers were involved in this phase. This phase was used for the final planning and preparation for the implementation of the project.

The following actions were carried out during this phase:

- Informed consent from care centre administrators and childrens' parents or legal guardians
- HIV screening
- The pilot project
- Changes and adaptations where necessary to study procedures, forms and questionnaires.
- Co-trimoxazole prophylaxis for all children, deworming
- Discontinue multi-vitamin supplementation: Week 0

3.10.2 Phase 2: Baseline data collection

All four researchers were involved in this phase. This phase included the following actions:

- Collection of baseline data by the different researchers
- Researcher 2 collected the baseline data for the anthropometric nutritional status (Addendum F).
- Researcher 4 collected baseline data for immune, biochemical and health status (Addendum H).
- Stratification and randomisation into the E and C-groups by the Department of Biostatitistics of the University of the Free State.

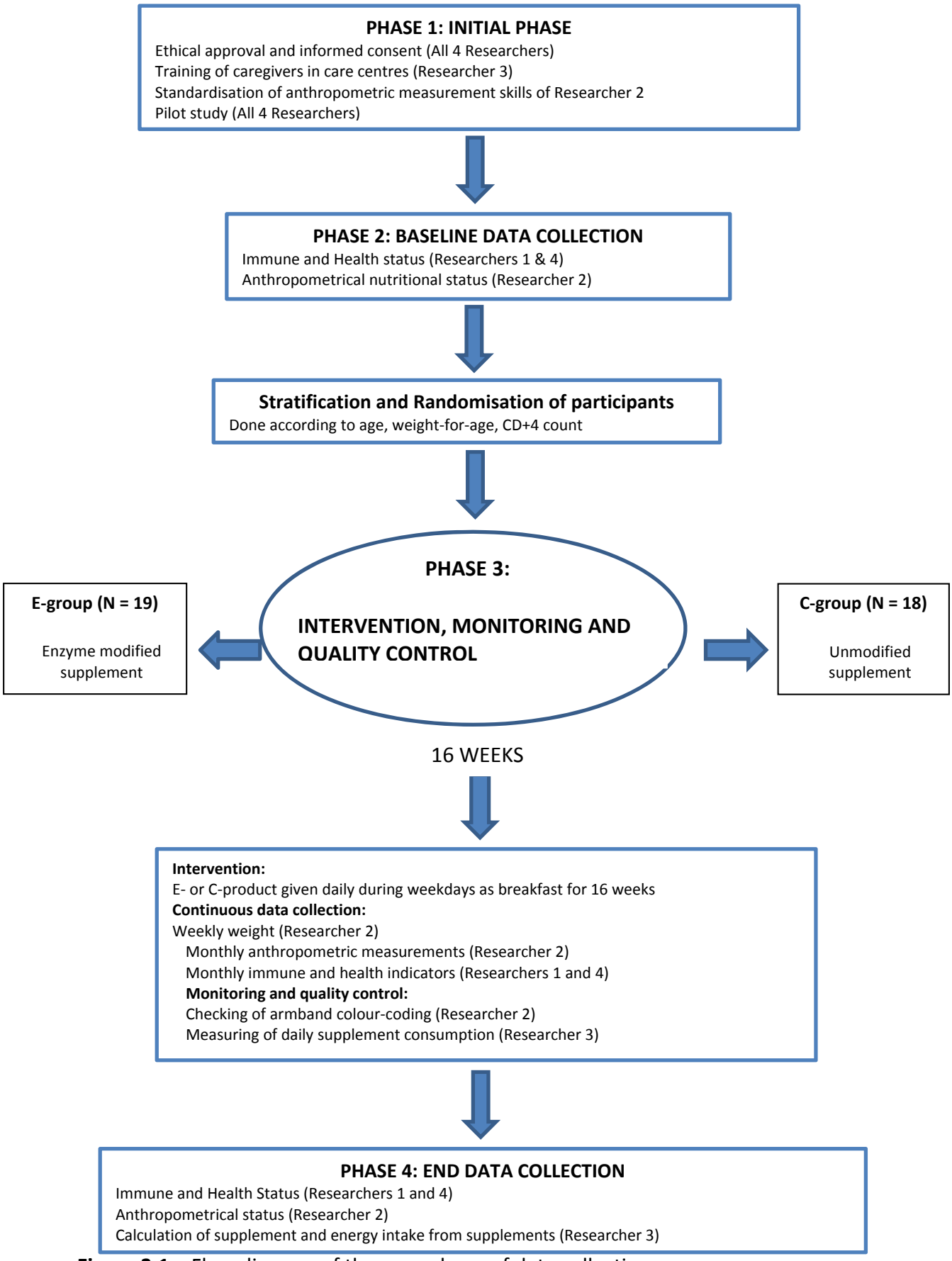


Figure 3.1: Flow diagram of the procedures of data collection

3.10.3 Phase 3: Intervention, monitoring and quality control

The intervention was done for a period of 16 weeks and consisted of a food supplement that replaced the usual breakfast in the care centres. Breakfast time was chosen because some of the children only attended day care at the facilities and did not eat supper at the facility. The supplementation products were also most suited as a breakfast food. No supplementation was given during weekends, as some of the children went home over weekends and researchers had little control over whether the children consumed the products or not.

Children in the E-group received the experimental product (an enzyme-modified, enriched supplement), and those in the C-group received the control product (an instant enriched supplement). A total of 150g (dry weight) of either the experimental or control product was provided to each child. The kitchen staff of the care centres was trained to mix each dry portion with 300 ml warm water and serve the correct product to each child.

Continuous data collection during the intervention period included weekly and monthly anthropometric measurements by Researcher 2 (Addendum C). Weight was measured weekly, on the last day of every week, early in the mornings, before the children had breakfast. Length/height, HC, MUAC and TSF measurements were taken 4-weekly (Addendum D).

Researcher 3 visited the two institutions on a daily basis to weigh the supplements (E and C) before and after consumption, to calculate actual supplement consumption by each child.

Researchers 1 and 4 gathered health status information on a 4-weekly basis (Addendum H).

Monitoring and quality control included checking of the colour-coding on the armbands that the children wore to indicate in which group they belonged. Confirmation of checking of colour-coding was noted on the form also used for weekly body weight measurements (Addendum C).

Researcher 3 was responsible for the quality control of the study; by making sure that each child received and consumed the correct supplement (experimental or control) and also the correct quantity of the relevant supplement.

3.10.4 Phase 4: Collection of End Data

After the intervention period of 16 weeks, all researchers collected the end data. End data that were collected, were the same as baseline data, and exactly the same procedures were followed as during the baseline data collection (Addendum G).

3.11 STATISTICAL ANALYSIS

Anthropometry was analysed using a CD-ROM pre-loaded with formulas on Excel spreadsheets for anthropometric status evaluations with WHO-, CDC- and NHANES III based anthropometric tables (Frisancho, 2008:VII-VIII).

Weight/height status Z-scores and percentiles were calculated using the WHO and CDC spreadsheets. Z-scores for weight/height status derived from the WHO spreadsheet were evaluated and classified according to WHO (WHO, 2008:14; 2009b:10) Z-score cut-off values. Z-scores for weight/height status derived from the CDC spreadsheets were evaluated and classified according to NCHS/CDC Z-score cut-off values for weight-height status.

Z-scores and percentiles for HC/A were calculated on the WHO spreadsheet. Percentiles for HC/A were evaluated and classified according to percentile cut-off values for HC/A and anthropometric nutritional status (Frisancho, 2008: 306, 314). Arm anthropometry Z-scores and percentiles were calculated on the Comprehensive reference (NHANES III based) spreadsheet (Frisancho, 2008:VII-VIII). Arm anthropometry percentiles were evaluated and classified according to percentile cut-off values for anthropometric nutritional status and arm anthropometry (Frisancho, 2008: 306, 314-317).

The statistical analysis was done by the Department of Biostatistics at the University of the Free State using the SAS statistical program. Descriptive statistics namely frequencies and percentages (categorical variables) and percentiles (numerical variables due to small sample sizes and skew distributions) were used to summarise baseline and end of study data of the groups. Anthropometric nutritional status of each group at baseline and at the end of the study was compared using 95% confidence intervals for changes in median values, as well as non-parametric sign rank tests and McNemar tests.

3.12 PROBLEMS ENCOUNTERED DURING THE STUDY

3.12.1 Small sample

Although the researchers expected to include 70 children in the study sample, only 37 could eventually be included. Of the 37 study children, 21.62% (n=8) dropped out. The drop-out percentage per group was 26.3% (n=5) for the E-group and 16.6% (n=3) for the C-group. Table 4.1 shows the age and gender distribution of the E- and C-groups at baseline and after completion of the intervention period.

Due to the small initial sample size and the drop-out percentage of 21.62% in the current study, interpretation of the results will be handled with great caution, in order to avoid misinterpretation.

3.12.2 Short intervention period

The researchers had to limit the intervention period to 120 days to avoid the impact of long school holidays. Most of the children visited family during the two long school holidays and if the study was continued over the holiday time, it would not be possible to monitor whether the children received regular meals as well as the supplements during this period. Weekly measurements of weight would also not be possible over the holiday periods.

Due to the limited time period available for the intervention, measurements of height at baseline as well as at the end of the study will be useful to interpret height status, but not to

measure the impact of the intervention on height status. In order to draw conclusions regarding the impact of nutrition intervention on height status, a longer intervention period of at least 6 months is needed. Impaired height growth is a result of chronic malnutrition over an extended period of time, and height growth over a short period (less than 6 months) of nutrition intervention cannot be interpreted as being the result of the intervention.

On the other hand, weight loss or poor weight status is a result of poor nutrition over a short period of time, especially in young children. Because weight loss is a symptom of short-term malnutrition, changes in weight can be interpreted as a result of nutrition intervention, even over short periods of intervention. Changes in weight status in this intervention study can therefore be used to assess the impact of nutrition intervention on the anthropometric nutritional status of this group of children.

3.12.3 Supplement not served over week-ends

Because the day-care centres linked to Sunflower care centre did not function over weekends, the supplement could only be served to the children 4 times per week. To compensate for this, the recommended 100g dry serving size was increased to 150g dry (450g reconstituted) serving for all the children. The majority of children did not have difficulty to consume the larger portion size. However, a few of the children with very poor appetite were not able to consume the full daily quantity in a single meal. To enable them to eat the full daily quantity of supplement, the 150g dry (450g reconstituted) portion was divided into two meals, namely a 75g dry (225g reconstituted) portion for breakfast time and a 75g dry (225g reconstituted) portion at lunchtime. The adaptation made it possible for these children to consume the full daily quantity of 150g dry (450g reconstituted). The reliability of the data was not influenced, as the children were eventually able to consume the full daily quantity. During the pilot study there were no children who were not able to consume the full daily quantity in one meal. Therefore, the adaptation was not made before the start of the main study as soon as it became clear that not all children could consume everything in one meal.

CHAPTER 4 - RESULTS

4.1 INTRODUCTION

The aim of the study was to determine the impact on the anthropometric nutritional status of HIV-infected children in care centres, with the use of an enzyme modified maize based enriched food supplement vs. the use of a maize based enriched food supplement that is not enzyme-modified. The results will be discussed in terms of weight/height status, HC and upper arm anthropometry.

4.2 SAMPLE DISTRIBUTION

The study was conducted in six care centres in the Mangaung area of Bloemfontein. All six centres focus on the care of HIV-infected or -affected children. Two of the centres, namely Lebone House Care Centre and Sunflower House Care Centre, are centres that provide full-time residence to HIV-infected and -affected children, while the other four are day care centres under the management of Sunflower House Care Centre.

The study population consisted of 37 antiretroviral naïve HIV-infected children from birth to 10 years, cared for in the mentioned care centres. HIV infection was determined using the ELISA test, and a viral load test done at baseline served as confirmation of the diagnosis. A total of 155 children were tested for HIV, and 37 were HIV-infected and included in the study.

After randomisation of the initial 37 children, 19 children were included in the E-group and 18 in the C-group (Table 4.1). Of the 19 children in the E-group, seven (36.8%) were female and 12 (63.1%) were male, and of the 18 children in the C-group, 8 (44.4%) were female and 10 (55.6%) were male. From the total study population at baseline, eight (21.6%) of the children were in the age group 12-47 months, 27 (73.0%) in the age group 48-107 months and two (5.4%) were in the age group 108-155 months. Only 29 children completed the intervention, eight dropped out before the end of the study. The reasons for dropping out are summarised in Chapter 3, Table 3.3.

TABLE 4.1 Age and gender distribution of the experimental and control groups at baseline and at the end of the intervention

AGE GROUP	E-GROUP								C-GROUP								TOTAL STUDY POPULATION (E-and C-group)		TOTAL STUDY POPULATION (E- and C-group)	
	BASELINE (n=19)				END (n=14)				BASELINE (n=18)				END (n=15)				BASELINE (n=37)		END (n=29)	
	Male		Female		Male		Female		Male		Female		Male		Female		M + F		M + F	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
1 – 3 years (12- 47 months)	3	25	2	28	2	25	2	33	2	20	1	12	2	22	1	16	8	22	7	24
4 – 8 years (48 – 107 months)	9	75	4	57	6	75	3	50	7	70	7	88	6	66	5	83	27	73	20	69
9 – 13 years (108 – 155 months)	0	0	1	14	0	0	1	17	1	10	0	0	1	11	0	0	2	5	2	7
Total by gender	12	100	7	100	8	100	6	100	10	100	8	100	9	100	6	100	37	100	29	100

4.3 ANTHROPOMETRIC NUTRITIONAL STATUS

The anthropometric nutritional status was evaluated using weight/height status, HC and upper arm anthropometry as a proxy.

The results of the anthropometric nutritional status will be described as a comparison between the baseline and the end values after intervention, for both the E-group and the C-group, including only the 14 children in the E-group and 15 in the C-group that have completed the study.

4.3.1 Weight/height status

The weight/height status was evaluated according to the WHO 2007 Growth Standards and the CDC 2000 Growth Reference Standards.

4.3.1.1 WHO Growth Standards

The frequency distribution of WAZ, HAZ and BMIZ for the E-group and C-group at baseline and at the end of intervention, according to the WHO Growth Standards (Frisancho, 2008: CD-ROM) and WHO Z-score cut-off values (WHO, 2008:14; 2009b:10) are indicated in Table 4.2.

According to Table 4.2, a total of 42.9% of the children in the E-group were underweight at the start of the intervention (14.3% severely underweight and 28.6% underweight). At the end of the intervention, the percentage of underweight children in the E-group remained at 42.9%. However, all the children were now in the underweight category and none in the severely underweight category. In the C-group, 42.9% of the children were underweight (28.6% severely underweight and 14.3% underweight) at the start of intervention, and 57.2% (14.3% severely underweight and 42.9% underweight) at the end of the intervention. In the E-group 57.2% (28.6% + 28.6%) of the children had WAZ in the normal weight ranges, both at the start and the end of the intervention, while in the C-group 57.1% started the

intervention in the normal weight range, and 42.9% had WAZ in the normal range at the end of intervention.

TABLE 4.2 Frequency of WAZ, HAZ and BMIZ for the experimental and control groups at baseline and at the end of intervention, according to the WHO Growth Standards (Frisancho, 2008: CD-ROM) and WHO Z-score cut-off values (WHO, 2008:14; 2009b:10) for malnutrition (WHO, 2008:14; WHO, 2009b:10)

Z-score (SD)	Category	E-group					C-group			
		Baseline		End			Baseline		End	
W/A		n=14	%	n=14	%		n=14*	%	n=14*	%
< -3	Severely underweight	2	14.3	0	0.0		4	28.6	2	14.3
<-2 - ≥-3	Underweight	4	28.6	6	42.9		2	14.3	6	42.9
<-1 to ≥-2	Normal weight	4	28.6	4	28.6		8	57.1	6	42.9
≥-1 to ≤1	Normal weight	4	28.6	4	28.6		0	0.0	0	0.0
> 1 to ≤2	Possible growth problem	0	0.0	0	0.0		0	0	0	0
H/A		n=14	%	n=14	%		n=15	%	n=15	%
< -3	Severely stunted	3	21.4	3	21.4		6	40.0	4	26.7
<-2 - ≥-3	Stunted	5	35.7	5	35.7		6	40.0	9	60.0
<-1 to ≥-2	Normal height	5	35.7	4	28.6		3	20.0	2	13.3
≥-1 to ≤1	Normal height	1	7.1	2	14.3		0	0.0	0	0.0
> 1 to ≤2	Normal height	0	0.0	0	0.0		0	0.0	0	0.0
BMI/A		n=14	%	n=14	%		n=15	%	n=15	%
< -3	Severely wasted	0	0.0	0	0.0		0	0.0	0	0.0
<-2 - ≥-3	Wasted	1	7.1	0	0.0		1	6.7	1	6.7
<-1 to ≥-2	Normal weight	3	21.4	1	7.1		2	13.3	2	13.3
≥-1 to ≤1	Normal weight	9	64.3	12	85.7		12	80.0	11	73.3
> 1 to ≤2	Possible risk of overweight	0	0.0	0	0.0		0	0.0	1	6.7
>2 to ≤3	Overweight	0	0.0	0	0.0		0	0.0	0	0.0
>3	Obese	1	7.1	1	7.1		0	0.0	0	0.0

* One of the children in the C-group was 122 months old at the end of the intervention, and is therefore not included.

In the E-group, 57.1% of the children were stunted (21.4% severely stunted and 35.7% stunted), both at the start and at the end of the study. In the C-group, 80% (40% severely stunted and 40% stunted) of the children were stunted at the start of the intervention, and 86.7% (26.7% and 60%) at the end of the intervention. A total of 42.8% (35.7% + 7.1%) of the children in the E-group had normal H/A, both at the start and at the end of intervention, while 20% of the children in the C-group had normal H/A at the start of intervention, and 13.3% at the end of the intervention.

At the start of the intervention, 85.7% (21.4% + 64.3%) of the children in the E-group had BMIZ in the categories that indicate normal weight. At the end of the intervention the percentage with normal BMIZ was 92.8% (7.1% + 85.7%). In the C-group, 93.3% (13.3% + 80%) of the children had normal BMIZ at the start of the intervention, and 86.6% (13.3% + 73.3%) at the end of the intervention.

Table 4.3 shows the Z-score medians, quartiles, minimum and maximum values and differences for the E- and the C-groups for WAZ, HAZ and BMIZ at baseline and at the end of intervention according to the WHO Growth Standards (Frisancho, 2008: CD-ROM) and WHO Z-score cut-off values (WHO, 2008:14; 2009b:10) for malnutrition.

TABLE 4.3 Medians, quartiles, minimums, maximums and differences for the experimental and control groups for WAZ, HAZ and BMIZ at baseline (start) and end of intervention, according to the WHO Growth Standards (Frisancho, 2008: CD-ROM) and WHO Z-score cut-off values (WHO, 2008:14; 2009b:10) for malnutrition

E-group									
Variable (WHO Growth Standards)		n	Median	Lower quartile	Upper quartile	Minimum	Maximum	Signed rank test p-value	95% CI for median of differences
WAZ	Start	14	-1.9	-2.4	-0.9	-3.9	0.5		
	End	14	-1.4	-2.5	-1.0	-3.0	0.7		
	Diff	14	0.2	0.0	0.4	-0.2	1.1	0.02	(-0.04;0.5)
HAZ	Start	14	-2.3	-3.0	-1.5	-4.1	-0.4		
	End	14	-2.2	-2.9	-1.4	-3.9	-0.1		
	Diff	14	0.1	0.1	0.3	-0.3	0.3	0.02	(0.02; 0.29)
BMIZ	Start	14	-0.8	-1.0	-0.1	-2.0	3.2		
	End	14	-0.6	-0.7	-0.1	-1.3	3.6		
	Diff	14	0.2	-0.1	0.5	-0.4	1.4	0.17	(-0.2; 0.7)
C-group									
Variable (WHO Growth Standards)		n	Median	Lower quartile	Upper quartile	Minimum	Maximum	Signed rank test p-value	95% CI for median of differences
WAZ	Start	14	-1.9	-3.4	-1.6	-4.9	-1.2		
	End	14	-2.2	-2.9	-1.0	-2.9	-1.0		
	Diff	14	0.2	-0.3	0.4	-0.5	0.9	0.54	(-0.4; 0.46)
HAZ	Start	15	-2.9	-3.7	-2.5	-6.3	-1.5		
	End	15	-2.8	-3.4	-2.2	-6.1	-1.3		
	Diff	15	0.2	0.1	0.2	-0.2	1.0	0.02	(0.1; 0.2)
BMIZ	Start	15	-0.1	-1.0	0.5	-2.7	1.0		
	End	15	-0.4	-0.9	0.2	-2.4	1.5		
	Diff	15	0.1	-0.5	0.5	-0.8	1.0	0.93	(-0.5; 0.5)

The difference in the median WAZ for the E-group was 0.2 Z-scores from the start to the end of the intervention, the difference in the medians for HAZ was 0.1, and for BMIZ the difference was 0.2 Z-scores. Although the differences for WAZ (p=0.02) and HAZ (p=0.02) were statistically significant, it was not clinically significant.

The median differences from the start to the end of the intervention for WAZ, HAZ and BMIZ in the C-group were 0.2, 0.2 and 0.1 Z-scores respectively. The difference in HAZ (p=0.02) was statistically significant, however, it was not clinically significant.

4.3.1.2 CDC 2000 Growth Reference Guidelines

The frequency distribution of WAZ, HAZ and BMIZ for the E- and C-groups at baseline and at the end of intervention, according to the CDC 2000 Growth Reference Guidelines (Frisancho, 2008: CD-ROM) and NCHS/CDC Z-score cut-off values (Lee & Nieman, 2010:169), are provided in Table 4.4.

A total of 78.6% of the children in the E-group were classified as underweight (14.3% severely underweight, 35.7% moderately underweight and 28.6% mildly underweight) at the start of the intervention. At the end of the intervention, the total in the underweight categories was the same (78.6%), but with a shift in categories to 14.3% severely underweight, 28.6% moderately underweight and 35.7% mildly underweight. In the C-group, all the children were underweight (33.3% severely underweight, 20% moderately underweight, and 46.7% mildly underweight) at the start and end of the intervention, with a shift in categories (33.3 severely underweight, 26.7% moderately underweight and 40% mildly underweight). A total of 21.4% of the children in the E-group had a normal WAZ at the start as well as at the end of the intervention, while no children in the C-group had WAZ in the normal weight range.

TABLE 4.4 Frequency of WAZ, HAZ and BMIZ for the experimental and control groups at baseline and at the end of intervention, according to the CDC 2000 Growth Reference Guidelines (Frisancho, 2008: CD-ROM) and NCHS/CDC Z-score cut-off values (Lee & Nieman, 2010:169) for malnutrition

Z-score (SD)	Category	E-group					C-group			
		Baseline		End			Baseline		End	
W/A		n=14	%	n=14	%		n=15	%	n=15	%
< -3	Severely underweight	2	14.3	2	14.3		5	33.3	5	33.3
<-2 to ≥-3	Moderately underweight	5	35.7	4	28.6		3	20.0	4	26.7
< -1 to ≥-2	Mildly underweight	4	28.6	5	35.7		7	46.7	6	40.0
≥-1 to≤2	Normal weight	3	21.4	3	21.4		0	0.0	0	0.0
>2	Overweight	0	0.0	0	0.0		0	0.0	0	0.0
H/A		n=14	%	n=14	%		n=15	%	n=15	%
< -3	Severely stunted	3	21.4	2	14.3		4	26.7	4	26.7
<-2 to ≥-3	Moderately stunted	5	35.7	5	35.7		8	53.3	7	46.7
< -1 to ≥-2	Mildly stunted	3	21.4	5	35.7		3	20.0	4	26.6
≥-1 to≤2	Normal height	3	21.4	2	14.3		0	0.0	0	0.0
>2	Above normal	0	0.0	0	0.0		0	0.0	0	0.0
BMI/A		n=14	%	n=14	%		n=15	%	n=15	%
< -3	Severely underweight	0	0.0	0	0.0		1	6.7	1	6.7
<-2 to ≥-3	Underweight	1	7.1	0	0.0		1	6.7	1	6.7
< -1 to ≥-2	Normal weight	5	35.7	3	21.4		2	13.3	2	13.3
≥-1 to≤2	Normal weight	7	50.0	10	71.4		11	73.3	11	73.3
>2	Overweight	1	7.1	1	7.1		0	0.0	0	0

A total of 78.5% of the children in the E-group were stunted (21.4% severely, 35.7% moderately and 21.4% mildly stunted) at the start of intervention. At the end of the intervention, 85.7% of the children in the E-group were stunted (14.3% severely, 35.7% moderately and 35.7% mildly stunted). In the C-group, all the children were stunted at the start of the intervention (26.7% severely, 53.3% moderately and 20% mildly stunted) and at the end of the intervention (26.7% severely, 46.7% moderately, 26.6% mildly stunted). The percentages of children with normal HAZ in the E-group were 21.4% at the start and 14.3% at the end of the intervention. None of the children in the C-group had normal HAZ at the start or at the end of the study.

A total of 85.7% (35.7% + 50%) of the children in the E-group had normal BMIZ at the start of the intervention. At the end of the intervention, 92.8% (21.4% + 71.4%) of the children in the E-group had normal BMIZ. In the C-group, a total of 86.6% (13.3% + 73.3%) of the children had BMIZ in the normal weight ranges, both at the start and at the end of the intervention.

Table 4.5 shows the Z-score medians, quartiles, minimum and maximum values and differences for the E- and C-groups for WAZ, HAZ and BMIZ at baseline and at the end of the intervention, according to the CDC 2000 Growth Reference Guidelines (Frisancho, 2008: CD-ROM) and NCHS/CDC Z-score cut-off values (Lee & Nieman, 2010:255) for malnutrition.

The median WAZ for the E-group had a difference of 0.2 Z-scores from the start of intervention to the end of the intervention. The median values for HAZ had a difference of 0.1 Z-scores, and the median values for BMIZ had a difference of 0.1 Z-scores from the start to the end of the intervention. These differences were, however not statistically significant.

The median WAZ for the C-group had a difference of 0.2 Z-scores from the start to the end of the intervention. The median difference in HAZ was 0.1 Z-scores and the median difference in BMIZ was 0.2 Z-scores. The p-values showed that the differences were not statistically significant.

TABLE 4.5 Medians, quartiles, minimums, maximums and differences for the experimental and control groups for WAZ, HAZ and BMIZ at baseline and at the end of intervention, according to the CDC 2000 Growth Reference Guidelines (Frisancho, 2008: CD-ROM) and NCHS/CDC Z-score cut-off values (Lee & Nieman, 2010:255) for malnutrition

E-group									
Variable (CDC Growth Reference)		n	Median	Lower quartile	Upper quartile	Minimum	maximum	Signed rank test p-value	95% CI for median of differences
WAZ	Start	14	-2.1	-2.7	-1.0	-4.7	0.7		
	End	14	-1.5	-2.7	-1.0	-3.5	0.9		
	Diff	14	0.2	0.1	0.5	-0.2	1.5	0.45	(0.4; 0.5)
HAZ	Start	14	-2.2	-2.9	-1.3	-3.6	-0.0		
	End	14	-2.2	-2.8	-1.2	-3.5	0.2		
	Diff	14	0.1	0.0	0.2	-0.3	0.4	0.23	(-0.1; 0.2)
BMIZ	Start	14	-0.8	-1.4	-0.1	-2.9	2.7		
	End	14	-0.7	-0.8	-0.2	-1.4	2.9		
	Diff	14	0.1	-0.1	0.7	-0.4	1.73	0.98	(-0.6; 0.6)
C-group									
Variable (CDC Growth Reference)		n	Median	Lower quartile	Upper quartile	Minimum	maximum	Signed rank test p-value	95% CI for median of differences
WAZ	Start	15	-2.1	-4.1	-1.7	-6.1	-1.2		
	End	15	-2.4	-3.4	-1.6	-6.7	-1.0		
	Diff	15	0.2	-0.4	0.5	-0.6	1.5	0.45	(-0.4; 0.5)
HAZ	Start	15	-2.7	-3.6	-2.1	-5.9	-0.0		
	End	15	-2.6	-3.1	-1.9	-5.9	0.2		
	Diff	15	0.1	-0.1	0.2	-0.3	0.4	0.23	(-0.1; 0.2
BMIZ	Start	15	-0.2	-1.5	0.3	-3.9	2.7		
	End	15	-0.4	-1.2	0.2	-3.3	2.9		
	Diff	15	0.2	-0.6	0.6	-1.0	1.7	1.0	(-0.6; 0.6)

4.3.1.3 Comparison of weight/height status using the WHO Growth Standards and cut-off values vs. CDC 2000 Growth Reference Guidelines and NCHS/CDC cut-off values

Both the WHO Growth Standards (Frisancho, 2008: CD-ROM) with WHO Z-score cut-off values (WHO, 2008:14; 2009b:10) for malnutrition and the CDC 2000 Growth Reference Guidelines (Frisancho, 2008: CD-ROM) with NCHS/CDC Z-score cut-off values (Lee & Nieman, 2007:255) for malnutrition were used to evaluate the weight/height status and the impact of the supplementation products on the study groups. The cut-off values for the two reference guidelines differ, as shown in Table 4.6.

TABLE 4.6 Comparison of WAZ, HAZ and BMIZ values using WHO Growth Standards (Frisancho, 2008: CD-ROM) with WHO Z-score cut-off values (WHO, 2008:14; 2009:10) for malnutrition vs. the CDC 2000 Growth ReferenceGuidelines (Frisancho, 2008: CD-ROM) with NCHS/CDC Z-score cut-off values (Lee & Nieman, 2003:347; 2007:255) for malnutrition

Z-score	WHO Definition	CDC Definition	E-group				C-group			
			Baseline %		End %		Baseline %		End %	
W/A			N=14	N=14	N=14	N=14	N=14	N=15	N=14	N=15
			WHO	CDC	WHO	CDC	WHO	CDC	WHO	CDC
< -3	Severely u/w	Severely u/w	14.3	14.3	0	14.3	28.6	33.3	14.3	33.3
<-2 to ≥-3	Underweight	Moderately u/w	28.6	35.7	42.9	35.7	14.3	20.0	42.9	26.7
< -1 to ≥-2	Normal weight	Mildly u/w	28.6	28.6	28.6	28.6	57.1	46.7	42.9	40.00
≥-1 to ≤1	Normal weight	N.A.	28.6	N.A.	28.6	N.A.	0	N.A	0	N.A
≥-1 to ≤2	N.A.	Normal weight	N.A.	21.4	N.A.	21.4	N.A	0	N.A	0
>1 to ≤2	Possible growth problem	N.A.	0	N.A.	0	N.A.	0	N.A	0	N.A
> 2	Possible growth problem	Overweight	0	0	0	0	0	0	0	0
>3	Possible growth problem	N.A.	0	N.A.	0	N.A.	0	N.A	0	N.A
H/A			N=14	N=14	N=14	N=14	N=15	N=15	N=15	N=15
			WHO	CDC	WHO	CDC	WHO	CDC	WHO	CDC
< -3	Severely stunted	Severely stunted	21.4	21.4	21.4	14.3	40.0	26.7	26.7	26.7
<-2 to ≥-3	Stunted	Moderately stunted	35.7	35.7	35.7	35.7	40.0	53.3	60.0	46.7
<-1 to ≥ -2	Normal height	Mildly stunted	35.7	21.4	28.6	35.7	20.0	20.0	13.3	26.7
≥-1 to ≤1	Normal height	N.A.	7.1	N.A.	14.3	N.A.	0	N.A.	0	N.A.
≥-1 to ≤2	N.A.	Normal height	N.A.	21.4	N.A.	14.3	N.A.	0	N.A.	0
>1 to ≤2	Normal height	N.A.	0	N.A	0	N.A	0	N.A	0	N.A
> 2	Normal height	Above normal	0	0	0	0	0	0	0	0
BMI/A			N=14	N=14	N=14	N=14	N=15	N=15	N=15	N=15
			WHO	CDC	WHO	CDC	WHO	CDC	WHO	CDC
< -3	Severely wasted	Severely u/w	0	0	0	0	0	6.7	0	6.7
<-2 to ≥-3	Wasted	Underweight	7.1	7.1	0	0	6.7	6.7	6.7	6.7
< -1 to ≥-2	Normal weight	Normal weight	21.4	35.7	7.1	21.4	13.3	13.3	13.3	13.3
≥-1 to ≤1	Normal weight	N.A.	64.3	N.A.	85.7	N.A.	80.0	N.A.	73.3	N.A.
≥-1 to ≤2	N.A.	Normal weight	N.A.	50.0	N.A.	71.4	N.A.	73.3	N.A.	73.3
>1 to ≤2	Possible risk of o/w	N.A.	0	N.A.	0	N.A.	0	N.A.	6.7	N.A.
> 2	Overweight	Overweight	0	7.1	0	7.1	0	0	0	0
>3	Obese	Obese	7.1	0	7.1	0	0	0	0	0

According to Table 4.6, the biggest difference between the WHO and NCHS/CDC classifications for W/A are the cut-off points for normal weight and underweight. The WHO classifies normal weight in the range WAZ ≥-2SD to <1SD, while the NCHS/CDC classification for normal weight is from WAZ >-1SD to ≤2SD. Due to these differences, the WHO classifies 57.2% (28.6% + 28.6%) of the children in the E-group with normal W/A, at the start as well as at the end of the intervention, while according to the NCHS/CDC classification only 21.4% of the children in the E-group had normal W/A at the start and at the end of the intervention. In the C-group the WHO classification system ranked 57.1% of the children with normal weight at the start of the intervention, and 42.9% at the end of the intervention. According to the NCHS/CDC classification none of the children in the C-group had normal W/A, because the NCHS/CDC cut-off values for mild underweight corresponds with one of the WHO cut-off values and Z-score ranges for normal weight.

The WHO classifies severe stunting as HAZ <-3SD, and the cut-off values for stunting is HAZ <-2SD to ≥-3SD. The NCHS/CDC classifies severe stunting as HAZ <-3SD, moderate stunting as HAZ <-2SD to ≥-3SD, and mild stunting as <-1SD to ≥-2SD. With these cut-off points, according to the WHO classification, 57.1% of the children in the E-group were stunted at both the start and end of the intervention. The NCHS/CDC system classified 78.5% of the children in the E-group as stunted at the start and at the end of the intervention. In the C-group the WHO system classified 80% of the children as stunted at the start of the intervention, and 86.7% at the end of the intervention. According to the NCHS/CDC system all the children in the C-group were stunted at the start as well as at the end of the intervention.

The WHO cut-off values for BMIZ is <-3SD for severe wasting, and BMIZ <-2SD to ≥-3SD for wasting. Normal weight is in the ranges BMIZ ≥-2SD through to ≤1SD. Above 1 SD (>1SD) indicates a possible growth problem. According to the NCHS/CDC classification, a BMIZ <-3SD indicates severe underweight, BMIZ <-2SD to ≥-3SD indicates underweight, BMIZ ≥-2SD through to ≤2SD indicates normal weight, and BMIZ above 2SD (>2SD) indicates overweight. According to both the WHO and NCHS/CDC classification systems, 85.7% of the children in the E-group had normal BMIZ at the start of intervention, and 92.8% at the end of the intervention. In the C-group, the WHO classification system classified 93.3% of the children

with normal BMIZ at the start of the intervention, and 86.6% at the end of the intervention. According to the NCHS/CDC classification system, 86.6% of the children in the C-group had normal BMIZ at the start as well as at the end of the intervention.

According to the WHO classification system, 7.1% (1 of 14) of the children in the E-group was wasted and 7.1% (1 of 14) was obese at the start of the intervention. According to the NCHS/CDC classification, 7.1% of the children in the E-group was underweight at the start of the intervention, and 7.1% was overweight. At the end of the intervention, the WHO system classified 7.1% of the children in the E-group as obese, and the NCHS/CDC classification system classified 7.1% as overweight. In the C-group, the WHO system classified 1 child (6.7% of 15) as wasted, both at the start and at the end of the intervention. The NCHS/CDC system classified 1 child (6.7% of 15) as severely underweight and 1 child (6.7% of 15) as underweight at the start as well as at the end of intervention.

4.3.2 Head Circumference

HC was expressed as percentile values for HC/A and evaluated according to the WHO Growth Standards (Frisancho, 2008:CD-ROM) and percentile cut-off values for anthropometric nutritional status and head circumference shown in Table 4.7 (Frisancho, 2008:306, 314).

TABLE 4.7 Percentile distribution for head circumference-for-age for the experimental and control groups according to the WHO Growth Standards (Frisancho, 2008:CD-ROM) and percentile cut-off values for the evaluation of anthropometric nutritional status and head circumference (Frisancho, 2008:306, 314)

Percentile	Description	E-group					C-group			
		Baseline		End			Baseline		End	
		n=9	%	n=9	%		n=10	%	n=10	%
<5	Small head circumference	1	11	1	11		4	40	5	50
≥ 5 to ≤ 14.9	Below average	1	11	1	11		1	10	0	0
≥15 to ≤ 84.9	Healthy	5	56	5	56		4	40	5	50
≥ 85 to ≤ 94.9	Above average	1	11	1	11		1	10	0	0
≥ 95	Large head circumference	1	11	1	11		0	0	0	0

HC was evaluated for the age group 12 to 72 months (Frisancho, 2008:CD-ROM). The HC of 19 of the study children could be evaluated (Table 4.7). HC was evaluated only as part of the total anthropometric evaluation of the study children, and was not used to evaluate the impact of the nutrition supplementation.

The HC/A of the majority of children in the E-group (56%) were in the healthy range at both the start and end of the intervention. In the C-group 40% of the children had small HC/A at the start of intervention, and 40% had HC/A in the healthy range. At the end of the intervention, 50% in the C-group had small HC/A and 50% had HC/A in the normal range.

Table 4.8 shows the percentile medians, quartiles, minimum and maximum values and differences for the HC/A in both the E- and C-groups at baseline and at the end of the intervention, according to the WHO Growth Standards (Frisancho, 2008:CD-ROM) and percentile cut-off values for anthropometric nutritional status and head circumference (Frisancho, 2008:306, 314). The median HC for the E-group had a difference of 0 Z-scores from the start to the end of the intervention. The median HC for the C-group had a difference of -0.2 from the start to the end of intervention. The p-values confirmed that the differences in HC were not significant.

TABLE 4.8 Medians, quartiles, minimums, maximums and differences for HC-for-age percentiles for the experimental and control groups at the start and at the end of intervention, according to WHO Growth Standards (Frisancho, 2008:CD-ROM) and percentile cut-off values for the evaluation of anthropometric nutritional status and head circumference (Frisancho, 2008:306, 314)

E-group									
HEAD CIRCUM-FERENCE		N	Median	Lower quartile	Upper quartile	Minimum	maximum	Signed rank test p-value	95% CI for median of differences
E-group	Start	9	46.1	31.1	69.5	3.6	99.9		
	End	9	34.9	31.1	69.5	2.4	99.9		
	Diff	9	0	-3.0	0	-11.4	3.33	0.31	(-1.2; 0.0)
C-group									
C-group	Start	10	13.2	1.5	44.9	0.2	87.7		
	End	10	12.5	0.8	44.9	0.2	84.2		
	Diff	10	-0.2	-0.7	0	-3.5	0	0.06	(-0.4; 0.0)

4.3.3 Upper arm anthropometry

Upper arm anthropometry was evaluated in terms of MUAC, TSF, UAMA and UAFA. MUAC, TSF, UAMA and UAFA were expressed as MUAC/A-, TSF/A-, UAMA/A- and UAFA/A percentiles and was evaluated according to the Comprehensive Anthropometric Reference based on the NHANES III for children and adults (Frisancho, 2008:VII, 112, CD-ROM) and the percentile cut-off values and categories for anthropometric nutritional status and arm anthropometry (Frisancho, 2008:306, 314-317) shown in Table 4.9.

The MUAC/A in the E-group were the same (healthy range 35.7%, below average 35.7% and low range 21.4% respectively) at the start and at the end of intervention. In the C-group at the start of the intervention the children fell in the healthy (40%), below average (33.3%) and low (26.7%) categories, while at the end of the intervention they fell in the low (40%), healthy (26.6%) and below average (13.3%) categories.

The TSF/A of the majority of the children in the E-group (71.4%) and C-group (86.7%) fell in the healthy range at both the start and end of the intervention.

The UAMA/A of the E-group at both the start and end of the intervention fell mainly in the below average (42.9% & 50% respectively) and healthy (21.4% & 35.7% respectively) ranges. In the C-group the UAMA/A of the majority also fell mainly in the below average (40% and 26.7%) and healthy ranges (40% and 53.3%), at the start as well as the end of the intervention.

The UAFA/A of the children in the E-group fell mainly in the below average (35.7%) and healthy ranges (35.7%) at the start of the intervention, and in the wasted (28.6%) and healthy ranges (42.9%) at the end of the intervention. In the C-group, the UAFA/A fell mainly in the wasted (40%) and healthy ranges (40%) at the start of the intervention, and in the below average (33.3%) and healthy ranges (46.7%) at the end of the intervention.

TABLE 4.9 Percentile distribution of MUAC/A, TSF/A, UAMA/A and UAFA/A for the experimental and control groups, at baseline and at end of intervention, according to the Comprehensive Anthropometric Reference based on the NHANES III for children and adults (Frisancho, 2008:CD-ROM) and the percentile cut-off values and categories for anthropometric nutritional status and arm anthropometry (Frisancho, 2008:306, 314-317)

Percentile	Category	E-group					C-group			
		Baseline		End			Baseline		End	
MUAC/A		N=14	%	N=14	%		N=15	%	N=15	%
<5	Low	3	21.4	3	21.4		4	26.7	6	40.0
≥ 5 to ≤ 14.9	Below average	5	35.7	5	35.7		5	33.3	2	13.3
≥15 to ≤ 84.9	Healthy range	5	35.7	5	35.7		6	40.0	7	26.6
≥ 85 to ≤ 94.9	Above average	0	0	0	0		0	0	0	0
≥ 95	Excessive	1	7.1	1	7.1		0	0	0	0
TSF/A		N=14	%	N=14	%		N=15	%	N=15	%
<5	Lean	2	14.3	2	14.3		0	0	0	0
≥ 5 to ≤ 14.9	Below average	1	7.1	1	7.1		0	0	0	0
≥15 to ≤ 84.9	Healthy range	10	71.4	10	71.4		13	86.7	13	86.7
≥ 85 to ≤ 94.9	Above average	0	0	0	0		1	6.7	1	6.7
≥ 95	Excess fat	1	7.1	1	7.1		1	6.7	1	6.7
UAMA/A		N=14	%	N=14	%		N=15	%	N=15	%
<5	Low muscle, wasted	4	28.6	2	14.3		3	20.0	3	20.0
≥ 5 to ≤ 14.9	Below average	6	42.9	7	50.0		3	40.0	4	26.7
≥15 to ≤ 84.9	Healthy range	3	21.4	5	35.7		9	40.0	8	53.3
≥ 85 to ≤ 94.9	Above average	1	7.1	0	0		0	0	0	0
≥ 95	High muscle, good nutrition	0	0	0	0		0	0	0	0
UAFA/A		N=14	%	N=14	%		N=15	%	N=15	%
<5	Wasted	3	21.4	4	28.6		6	40.0	3	20.0
≥ 5 to ≤ 14.9	Below average	5	35.7	3	21.4		2	13.3	5	33.3
≥15 to ≤ 84.9	Healthy range	5	35.7	6	42.9		6	40.0	7	46.7
≥ 85 to ≤ 94.9	Above average	0	0	0	0		1	6.7	0	0
≥ 95	Excess fat	1	7.1	1	7.1		0	0	0	0

Table 4.10 shows the percentile medians, quartiles, minimum and maximum values and differences for the MUAC/A, TSF/A, UAMA/A and UAFA/A percentiles in the E- and C-groups at the start and at the end of the intervention, according to the Comprehensive Anthropometric Reference based on the NHANES III for children and adults (Frisancho, 2008:CD-ROM) and the percentile cut-off values and categories for anthropometric nutritional status and arm anthropometry (Frisancho, 2008:306, 314-317).

TABLE 4.10 Percentile medians, quartiles, minimums, maximums and differences for MUAC/A, TSF/A, UAMA/A and UAFA/A in the experimental and control groups at baseline and end, according to the Comprehensive Anthropometric Reference based on the NHANES III for children and adults (Frisancho, 2008: CD-ROM) and the percentile cut-off values and categories for anthropometric nutritional status and arm anthropometry (Frisancho, 2008:306, 314-317)

E-group									
Variable (NHANES III Based)		N	Median	Lower quartile	Upper quartile	Minimum	maximum	Signed rank test p-value	95% CI for median of differences
MUAC	Start	14	13.0	8.6	35.8	0	99.1		
	End	14	11.4	5.9	28.8	0	98.2		
	Diff	14	-2.1	-3.2	-0.1	-7.1	0	0.00	(-5.2; 0)
TSF	Start	14	39.3	27.4	57.7	1.9	96.0		
	End	14	37.8	24.6	55.7	1.9	96.0		
	Diff	14	0	-2.0	0	-2.9	0	0.03	(-2.7; 0)
UAMA	Start	14	11.7	3.6	30.5	2.2	89.6		
	End	14	9.8	8.1	20.1	2.4	62.2		
	Diff	14	0.18	-3.6	3.6	-27.4	8.2	1.00	(-6.2; 6.1)
UAFA	Start	14	13.3	6.7	20.1	0	96.7		
	End	14	15.5	4.3	40.9	0	99.9		
	Diff	14	3.2	-0.4	9.0	-9.4	20.8	0.13	(-1.5; 13.1)
C-group									
Variable (NHANES III Based)		N	Median	Lower quartile	Upper quartile	Minimum	maximum	Signed rank test p-value	95% CI for median of differences
MUAC	Start	14	11.1	1.9	26.7	0.2	73.1		
	End	14	9.2	2.9	22.7	0.2	66.7		
	Diff	14	-2.1	-3.2	-0.1	-7.1	6.5	0.02	(-5.1; -0.3)
TSF	Start	14	50.3	32.5	67.0	17.3	96.3		
	End	14	48.9	33.6	66.2	15.9	95.1		
	Diff	14	0	-1.9	0	-2.9	3.5	0.25	(-1.4; 0)
UAMA	Start	14	22.5	7.0	31.5	2.2	46.9		
	End	14	18.7	8.9	30.9	0.8	59.2		
	Diff	14	0.2	-3.6	3.6	-27.4	16.9	0.64	(-4.2; 2.3)
UAFA	Start	14	11.3	0.1	41.1	0.0	92.7		
	End	14	14.5	9.5	39.3	0	63.3		
	Diff	14	3.2	-0.4	9.0	-9.4	27.9	0.23	(-3.7; 11.0)

The difference in the median values for MUAC/A in the E-group was -2.1 percentile values from the start of intervention to the end of the intervention, and 0.00, 0.18 and 3.2 for TSF/A, UAMA/A and UAFA/A respectively. Although the differences in the MUAC/A ($P<0.05$) and TSF/A ($P<0.05$) in the E-group were statistically significant, they were not clinically significant.

The differences in the median values for in the C-group were -2.1, 0.0, 0.2 and 3.2 percentile values for MUAC/A, TSF/A, UAMA/A and UAFA/A respectively. Although the p-values for the median differences for MUAC ($P<0.05$), was statistically significant, it was not clinically significant.

4.4 SUMMARY

This study was carried out to measure the impact of an enriched, maize-based food supplement with added α-amylase on the anthropometric nutritional status of HIV-infected children in care centres in the Mangaung area of Bloemfontein in the Free State Province. A total of 37 HIV-infected children aged 1 to 10 years were selected for the intervention, of whom 29 children completed the intervention.

When comparing to the WHO Growth Standards and cut-off values for malnutrition (Table 4.2), 42.9% of the children in both the E- and C-group were underweight for age at the start of the intervention. At the end of the intervention, 42.9% in the E-group and 57.2% in the C-group were underweight for age. The majority of children were stunted in the E-group (57.7% at the start and end of the intervention) as well as in the C-group (80% at start and 85.7% at end). BMI/A was normal for most of the children in the E-group (85.7% at the start of intervention, and 92.8% at the end), as well as in the C-group (93.3% at the start and 86.6% at the end of intervention).

According to the CDC 2000 Growth Reference and the NCHS/CDC classification (Table 4.4), 78.6% of the children in the E-group were underweight for age at both the start and end of the intervention. All the children in the C-group were underweight. Most of the children in the E-group were stunted at the start (78.6%) and end (85.7%) of the study. All the children in the C-group were stunted at both the start and at the end of the study. The majority of children in both the E-group (86.7% at start and 92.8% at end) and the C-group (86.6%) had a normal BMI/A at baseline and end of intervention.

The WHO Standards (Table 4.6) classified fewer children as underweight and stunted than the NCHS/CDC classification system. The classifications for BMI/A with the WHO and the

NCHS/CDC classification systems were very similar, where the majority of children were classified with normal BMI/A (WHO: E-group 85.7% start and end, C-group 93.3% start, 86.6% end, NCHS/CDC: E-group 86.7% start, 92.8% end, C-group 86.6% start and end).

The HC/A (Table 4.8) for the majority of children in the E-group was normal (56%) at the start and end of the study, and for the C-group 40% had normal HC/A at the start and 50% at the end of intervention.

The MUAC/A (Table 4.9) of the E-group fell mainly in the healthy (35.7%) and below average (35.7%) ranges at the start and at the end of intervention. In the C-group the children fell in the healthy (40%), below average (33.3%) and low (26.7%) categories at the start of the intervention, and in the low (40%), healthy (26.6%) and below average (13.3%) categories at the end of the intervention.

The TSF/A (Table 4.9) of the majority of the children in the E-group (71.4%) and C-group (86.7%) fell in the healthy range, both at the start and end of the intervention.

The UAMA/A (Table 4.9) of the E-group fell mainly in the below average (42.9% & 50% respectively) and healthy (21.4% & 35.7% respectively) ranges at the start and end of the intervention. In the C-group the UAMA/A of the majority was in the below average (40% and 26.7%) and healthy ranges (40% and 53.3%), at the start as well as the end of the intervention.

The UAFA/A (Table 4.9) of the children in the E-group fell mainly in the below average (35.7%) and healthy ranges (35.7%) at the start of the intervention, and in the wasted (28.6%) and healthy ranges (42.9%) at the end of the intervention. The UAFA/A of the C-group fell mainly in the wasted (40%) and healthy ranges (40%) at the start of the intervention, and in the below average (33.3%) and healthy ranges (46.7%) at the end of the intervention.

No clinically significant changes in anthropometric nutritional status were seen between the baseline and end results within either the E- or the C-groups. Also, there was no significant difference between the anthropometric status of the E- and C-groups.

CHAPTER 5 - DISCUSSION

5.1 INTRODUCTION

This study was carried out to determine the impact of an enzyme modified, enriched maize based supplement on the anthropometric nutritional status of anti-retroviral naïve, food secure but economically deprived, HIV-infected children in care centres in Mangaung in the Free State Province. The most important observations regarding the anthropometric nutritional status of the children at baseline and at the end of intervention is discussed in the light of the limitations of the study and compared to other studies.

5.2 LIMITATIONS OF THIS STUDY

The small sample size of 37 children of whom 8 dropped out during the course of the intervention, was the biggest limitation of this study. Only 29 (E=14; C=15) children completed the study. Due to the small sample size, the results of this study should be interpreted with some caution. Practical arrangements around school holidays and day-care centres that are closed over weekends, limited the intervention period to 120 days, in addition to having only four days per week to serve the supplement. Monitoring of supplement consumption and weekly anthropometric measurements would not have been possible if the intervention was extended over the holiday time, which could have had an additional impact on the outcome of the study Even though the children in this study were considered to be food secure (due to either residence in a care centre or attendance of a day-care centre), they were from economically deprived families. It is unknown whether this social status had an independent impact on the outcome of the study.

The study was carried out in six care centres simultaneously, leading to the researchers having to rely heavily on the staff of the centres for the correct preparation of the supplements. All staff employed by these facilities was trained intensively and monitoring and control measures were put into place to monitor adherence to the protocol. Yet, even though everything was done to make sure that the study protocol was followed, the researchers still had to rely and depend on the willingness and commitment of the staff at

the participating facilities, which is difficult to control unless the researchers are present at all times, which was not possible in this study.

5.3 ANTHROPOMETRY AT BASELINE

The results of only the 29 HIV-infected participants who completed the intervention are discussed. The mean (SD) age of the 29 children at baseline was 64.1 months (23.6 months). Children in the E-group received the E-product (enzyme modified) and those in the C-group the C-product (no added enzyme).

5.3.1. Weight-for-age

HIV infection in children is associated with growth failure and increased mortality (Bailey *et al*., 1999:535; Arpadi *et al*., 2000:2501; Maleta *et al*., 2003:389; Newell *et al*., 2003:e57; Villamor *et al.*, 2005:66). Babies born to HIV-infected mothers tend to have a mean weight that is less than that of babies not infected with HIV (Saavedra *et al*., 1995:497; Lepage *et al*., 1996:479; Bobat *et al.,* 2001:207; Venkatesh *et al*., 2010:1366-7; Kimani-Murage *et al.*, 2011:23), and their W/A stay behind that of uninfected children as they grow older (McKinney *et al*., 1993:580; Bailey *et al*., 1999:535-7; Bobat *et al.,* 2001:207). Saavedra *et al*. (1995:499) reported that the difference in WAZ between HIV-infected and non-infected children became especially noticeable from age 36 months. In the European Collaborative Study it was found that differences in W/A become especially prominent by four years of age, and by age 8 and 10 years, children infected with HIV weighed on average 7 kg less than those not infected with HIV (Newell *et al*., 2003:e57). In the current study, where the oldest child was 10 years and the youngest 12 months, the children in the E-group were on average 3.4 kg lighter than the mean weight for age, and those in the C-group 4.2 kg. In the current study, there was no clear pattern showing that older children (eight to 10 years) or children older than three to four years had body weights that differed more from the mean weight for age than the younger children. The European Collaborative Study was carried out amongst children in eight European countries, and the British Growth Standards were used for evaluation of their anthropometric nutritional status. Differences in growth between ethnical groups could have played a role in the differences between the European children

and those in the current study population. Differences between the British Growth Standards and the WHO Growth Standards used in the current study could also contribute to the different results found in the current study. What is of importance, however, is that the children in the current study did have WAZ below the means for their age groups.

In the current study, 42.9% of the children in both the E- and C-group were underweight at baseline, according to the WHO Growth Standards and cut-off values for malnutrition (Table 4.2). Each group had 57.2% children with normal WAZ (≥-2SD to ≤1SD). The CDC 2000 Growth Reference Guide with NCHS/CDC cut-off values classified 78.6% of the children in the E-group and all the children in the C-group as underweight for age (<-3SD to <-1SD) at baseline.

Similar high percentages of children classified with underweight for age was reported by other studies amongst HIV-infected children in other provinces. At the immunology outpatient clinic of Livingstone Hospital in the Eastern Cape, 50.9% out of 102 HIV-infected, anti-retroviral naïve preschool children aged 18 to 72 months (mean age 40.7 months), were underweight for age (WAZ <-2SD) (Steenkamp *et al.*, 2004:unpublished). In the abovementioned study, no significant difference was found between the mean WAZ scores of food secure and food insecure children (food security as reported by children's carers). The children were on the standard treatment regimen for HIV-infected children according to the government protocol at the time of the study, namely co-trimoxazole prophylaxis, treatment of opportunistic infections, therapeutic doses of Vitamin A every 4 to 6 months, and a daily multivitamin supplement.

Eley *et al*. (2002:19) reported 28% underweight (WAZ <-2SD, NCHS anthropometric guidelines) amongst 60 healthy, stable, economically deprived, HIV-infected children (median age 25 months) attending the HIV clinic at the Red Cross War Memorial Children's Hospital in Cape Town. The lower median age (25 months) of the children in the study by Eley *et al*. (2002:20) as compared to the mean (SD) age of 64.1 months (23.6 months) of the current study probably played a role in the lower percentage of underweight for age compared to the current study group, since WAZ in HIV-infected children is more prominently influenced after age 36 months (Saavedra *et al*., 1995:499) or 48 months

(Newell *et al*., 2003:e52). The fact that the Cape Town study specifically targeted healthy, stable HIV-infected children, could also explain the lower percentage of WAZ. Although HIV-infected children in general grow slower than non-infected children, associated illnesses consistently worsen already delayed growth in W/A (Bailey *et al*., 1999:537).

Statistics on ill, HIV-infected children aged one to 59 months, admitted (with pneumonia, gastro-enteritis, TB) to Chris Hani Baragwanath Hospital from October 2007 to December 2007, shows 55.3% severe underweight (WAZ <-3SD) on admission (Dramowski *et al*., 2011:20). In the study by Steenkamp *et al*. (2004) where the percentage of underweight was 50.9%, children with lower Z-scores had decreased food intake (due to illness), chronic diarrhoea, HIV symptoms and TB symptoms. Newell *et al*. (2003:e58) also found that children with severe HIV symptoms had lower WAZ than those with mild/moderate symptoms or asymptomatic children. The health status of the children in the current study was evaluated by Researcher 1 (Steenkamp *et al*., 2009:133), using several evaluation systems which included the WHO Clinical Staging for Infants and Children with established HIV Infection. Only four of the children were classified with Clinical Stage 1, seven each with Stage 2 and 3, and 19 with Stage 4 (37 children, including eight drop-outs). The relatively poor health status of this group of children may explain the 42.9% children classified as underweight in this study.

The incidence of malnutrition in groups of unknown HIV status is lower when compared to studies targeting HIV-infected children. A study of the anthropometric nutritional status of preschool children (younger than 72 months) in two informal settlements in the Mangaung area classified 19.8% and 18.6% of the children as underweight for age (WAZ <-2SD, using NCHS reference guidelines) (Dannhauser *et al*., 2000:303).

National studies in South Africa where HIV status was not taken into consideration, found 13.6% (WAZ <-2SD) and 2.4% (WAZ <-3SD) underweight in children aged 6 – 71 months in the Free State Province, and 9.3% (WAZ <-2SD) and 1.4% (WAZ <-3SD) in the total Republic of Soutth Africa (RSA) (SAVACG, 1996:102). In 1999, the prevalence of underweight amongst children aged 1 to 9 years was 10.3% for the RSA (NFCS, 2000:193), and in 2005 the

prevalence in the same age group was 9.3% (NFCS-FB, 2007:144). NCHS 1977 Growth Reference Guidelines were used in these studies.

The median WAZ of the current study population (Table 4.3) (E-group -1.9SD; C-group -1.9SD, using WHO Growth Standards) at baseline indicated normal weight, although the values were very close to the -2SD cut-off value. A few published studies could be found that specifically evaluated nutritional status of HIV-infected children in the age group 1 to 10 years in the RSA. The percentage of underweight (42.9%) in the current study, where the majority of children were classified with WHO Clinical Stage 3 and 4 HIV, was higher than the 28% found in healthy HIV-infected children in a study by Eley *et al*. (2002:19), but lower than the 50.9% found by Steenkamp *et al.* (2004:unpublished) in children at a HIV clinic in the Eastern Cape who had symptoms of HIV progression. The percentage children found underweight for age in the present study population was also lower than the percentage of severely underweight children (55.3% admitted for hospitalisation in Gauteng (Dramowski *et al*., 2011:20).

5.3.2 Height-for-age

Stunting in HIV-infected children is correlated with increased viral replication and disease progression, and increased risk of death (Pollack et al., 1997:919; Bailey *et al*., 1999:535; Arpadi *et al*., 2000:2501; Benjamin *et al.*, 2003:2331; Newell *et al*., 2003:e57; Villamor *et al*., 2005:66). Stunting has been identified as a strongly reliable instrument (ranked first of 11 factors) to evaluate and monitor the nutritional risk of children infected with HIV (Heller *et al*., 2000:326). In a clinical trial by Benjamin *et al*. (2003:233-5) where HIV-infected children aged 3 to 18 years were treated with ARV medications, nutritional status was evaluated as part of the treatment outcome. It was found that in children with improved HAZ (due to ART), viral count and clinical progression of HIV was reduced significantly (in comparison to before treatment), thereby significantly reducing the risk of early death.

A lower mean HAZ is reported in HIV-infected children born to HIV-infected mothers, compared to uninfected children born to HIV-infected mothers in South African (Saavedra *et al.,* 1995:499; Bobat *et al.,* 2001:207; Webb *et al*., 2008:88; Venkatesh *et al*., 2010:1368;

Kimani-Murage *et al.*, 2011:23) as well as in international studies (McKinney *et al*., 1993:581; Pollack *et al*., 1997:917; Bailey *et al*., 1999:535; Newell *et al*., 2003:e52; Webb *et al*., 2008:87) .

Stunting caused by HIV infection through MTCT starts very early in life. Some researchers identified low H/A already in the first three months (Pollack et al., 1997:919,920), others during the first 20 months (Bailey *et al.*, 1999:537). The differences in height growth become more prominent as the child grows older. In the European Collaborative Study the biggest difference in height growth started around two years of age, and by age 10 years, the HIV-infected children were on average 7.5 cm shorter than those not infected with HIV (Newell *et al*., 2003:e52). In the current study, the children in the E-group were on average 10 cm shorter than the mean H/A of the reference population (per age group), and those in the C-group were on average 14.3 cm shorter than the mean H/A of the reference population. These drastic differences between the child's H/A and the mean H/A for the child's age group were distributed throughout the age ranges of the two groups. No pattern of larger differences in specific age groups could be identified.

In the current study, 57.1% of the children in the E-group and 80% of the children in the C-group were stunted at baseline, while only 42.8% in the E-group and 20% in the C-group had normal HAZ at baseline (Table 4.2) (according to WHO Growth Standards and cut-off values). The NCHS/CDC classification system classified 78.5% of the children in the E-group and all the children in the C-group as stunted at baseline.

A similar high (58.8%) percentage of stunting (HAZ <-2SD) was demonstrated amongst 102 HIV-infected, anti-retroviral naïve preschool children aged 18 to 72 months (mean age 40.7 months) at the immunology outpatient clinic of Livingstone Hospital in the Eastern Cape (Steenkamp *et al.*, 2004:unpublished), as well as amongst 60 stable, economically deprived, HIV-infected children (median age 25 months) attending the HIV clinic at the Red Cross War Memorial Children's Hospital in Cape Town (Eley *et al*., 2002:19). Kimani-Murage (2011:4) found a lower (29%) percentage of stunting amongst rural South African HIV-infected children aged 12 to 59 months in the rural Agincourt sub-district of the Mphumalanga Province.

Amongst preschool children of unknown HIV status in two informal settlements in the Mangaung area, 29% and 21.5% of the children were stunted (Dannhauser *et al*., 2000:303). In children of unknown HIV status, aged 6-71 months, residing in the Free State Province in 1994, 28.7% had HAZ <-2SD and 8.6% had HAZ <-3SD. In the total Republic of South Africa, (RSA), amongst children in the same age group (6 - 71 months), the prevalence of stunting was 22.9% (<-2SD) and 6.6% (<-3SD) (SAVACG, 1996:102). In 1999, the prevalence of stunting amongst children aged 1 to 9 years was 21.6% for the RSA (NFCS, 2000:193), and in 2005 the prevalence in the same age group was 18% (NFCS-FB, 2007:144). The NCHS 1977 Growth Reference Guidelines were used in the studies of SAVACG and the two National Food Consumption Survey (NFCS) studies for evaluation of anthropometric nutritional status.

The median HAZ (Table 4.3) (E-group -2.3SD; C-group -2.9SD) of the children in the present study confirms the high percentage of stunting. The percentage of stunting in the present study compares with the 58.8% that was reported in a study by Steenkamp *et al*. (2004:unpublished) amongst HIV-symptomatic children in the Eastern Cape, but is high in comparison to the prevalence in national studies amongst children of unknown HIV status. This is in accordance with the findings of other researchers that HIV-infected children are more stunted than non-infected children. The high percentage of stunted children in the current study may be linked to the relatively poor health status of the children (5.2.1), since stunting has been identified as a high risk factor for disease progression in HIV-infected children.

5.3.3 BMI-for-age

Low BMI/A is a highly reliable measure of malnutrition in HIV-infected children (Heller *et al*., 2000:326). In adults, an abrupt decline in BMI is usually a sign of progression to AIDS (Maas *et al*., 1998:254). BMI/A Z-scores of HIV-infected infants and children born to HIV-infected mothers are lower when compared to that of non-infected children. Within the group of HIV-infected children who participated in the European Collaborative study, HIV asymptomatic children and those with only mild to moderate symptoms, had higher (healthier) BMI/A Z-scores than those with severe symptoms, illustrating that the

detrimental impact of HIV on growth is exacerbated in the presence of HIV/AIDS (Newell *et al*., 2003:e57).

In the current study, the WHO classification (Table 4.2) placed 85.7% of the children in the E-group and 93.3% of the C-group in the normal BMIZ/A ranges. Classification according to the NCHS/CDC system placed 85.7% in the E-group and 86.6% in the C-group in the normal range for BMI/A.

The median BMIZ (Table 4.3) (E-group -0.8SD; C-group -0.1SD) indicated a normal weight for the majority of children in the current study. This is reflected in the high percentage of children classified with a normal BMI/A (E-group 85.7%; C-group 93.3%). The percentage of children with normal BMI/A in the present study is higher than the percentage with normal W/A (42.9% E- and C-group respectively) in the study group, which can be explained in the sense that BMI/A is an expression of weight relative to height, and that the majority of the children were stunted.

5.3.4 Head circumference

HC changes most rapidly during the first two years of life, and during this time the measurement of HC is a useful tool to monitor child brain growth (Gibson, 2005:254; Frisancho, 2008:313; Lowenthal & Phelps, 2009:Online). Head circumference-for-age can be used as a routine measurement of growth up to the age of 36 months (Lee & Nieman, 2010:163), and as an evaluation tool for variability in brain growth and the risks associated with it, from birth up to seven years (Frisancho, 2008:7-8, 313-4).

In the current study, HC/A of children up to the age of six years was evaluated (Table 4.7). The majority (56%) of the children in the E-group and 40% in the C-group had HC/A in the healthy range. In a study by Eley *et al*. (2002:21) 29% of the children younger than 36 months had HC below the 5th percentile. In the present study, only five of the 29 children were younger than 36 months, and three (60% of five) children had HC below the 5th percentile. Although this figure may be distorted due to the small sample size of the present study, the fact that some of the children did have low H/A deserves mentioning.

The median HC/A of the E-group (46th percentile) was in the healthy range, but the C-group had a median HC/A in the "below average" range (13.2th percentile).

In summary, the children in the C-group had a poorer anthropometric nutritional status in terms of HC/A than the children in the E-group. Due to the small sample size, the HC/A for the present study was not compared with other studies.

5.3.5 Upper arm anthropometry

MUAC, TSF and UAMA reflect fat and lean body mass stores (Heller, 1997:473). Miller *et al*. (1993:588) reported that HIV-infected children had significantly less lean body mass (as determined by MUAC and TSF assessments) than control children of the same age.

In the present study, the MUAC/A (Table 4.9) of 35.7% of the children in the E-group and 40% of the C-group was in the healthy range (≥15 to ≤84.9th percentile) at baseline. The percentage with MUAC/A below the 5th percentile was 21.4% in the E-group and 26.7% in the C-group. In a study of preschool children (younger than 72 months) of unknown HIV status in two informal settlements in the Mangaung area, 14.6% and 12.3% of the children were reported to have a MUAC/A that fell below the 5th percentile (Dannhauser *et al*., 2000:303). In the present study, 72.4% (E-group: 57.1%; C-group: 86.6%) of the children were younger than 72 months. The higher percentage of children with low MUAC/A in the present study compared to the study by Dannhauser *et al*. (2000:303), can possibly be ascribed to poorer nutritional status due to the HIV-infection.

TSF measurements provide an estimate of the size of the subcutaneous fat depot. Results of this study indicates that the majority (E-group 71.4%, C-group 86.7%) of children in both groups had triceps skinfolds that fell in the healthy range, which is confirmed by the results of the MUAC/A measurements of the children included in the current study (Table 4.9). The percentage of healthy triceps skinfold in the present study is higher than the 57% and 66.9% that was measured in preschool children (HIV status unknown) in two informal settlements in the Mangaung area (Dannhauser *et al*., 2000:303).

UAMA can be used in calculating total body muscle mass. In the current study, 28.6% of the children in the E-group and 20% of the C-group had an UAMA that falls below the 5th percentile (Table 4.9). In preschool children of unknown HIV status in two informal settlements in the Mangaung area, 8.1% and 6.6% had an UAMA below the 5th percentile (Dannhauser *et al*., 2000:303). The higher number of children with an UAMA that falls below the 5th percentile in the present study group, can be interpreted as poorer muscle growth in children infected with HIV compared to those not infected. This agrees with Fontana *et al*. (1999:1284) who reported lower fat free mass (FFM) and UAMA in HIV-infected children, and Miller *et al*. (1993:588) who reported less lean body mass in HIV-infected children as opposed to non-infected children of the same age. The interpretation should, however, be done with caution, since the children in the study by Fontana *et al.* (1999:1284) were white and aged birth to 15 years.

UAFA can also be used to derive an estimate of total body fat. In the current study, the E-group had 21.4% children with UAFA less than the 5th percentile, and the C-group 40% (Table 4.9). In preschool children (younger than 72 months, unknown HIV status) in two informal settlements in the Mangaung area, the percentage with UAFA below the 5th percentile was 12.6% and 11.6% respectively (Dannhauser *et al*., 2000:303), which is lower than in the present study. This supports the findings of other researchers that growth is impaired in HIV-infected children. The high percentage of 40% with UAFA below the 5th percentile in group C does, however, not correspond with the TSF/A that was found to be mostly normal.

The median percentile values for the upper arm anthropometry of the E-group showed below average status for MUAC (13.0th percentile), UAMA (11.7th percentile) and UAFA (13.3th percentile), indicating lower than optimum muscle and fat mass in this group of children. The median percentile values of the C-group showed below average status for MUAC (11.1th percentile) and UAFA (11.3th percentile), indicating lower than optimum fat mass.

In summary, the anthropometric nutritional status of both the E- and C-group children in terms of upper arm anthropometry was mainly below average at baseline. The results may support the findings of other researchers that growth in HIV-infected children is impaired, since weight status and body weight, which are both influenced by HIV-infection, is a combination of both lean and fat mass.

5.4 ANTHROPOMETRY AFTER INTERVENTION

Anthropometric nutritional status did not change significantly in either the E- or the C-group.

In an intervention study by Oelofse *et al*. (2003:399-407) in the Western Cape, a micronutrient-fortified maize-based supplement was used for six months in a randomised, controlled trial in children aged six to 12 months. The children were of unknown HIV status and not necessarily malnourished. No benefit was observed in terms of weight gain or growth in height. The researchers concluded that the relative good anthropometric nutritional status of the children in the study group may have contributed to the absence of significant changes in weight status, and that the intervention period of six months was too short for significant changes in height status. In the present study, the study children did not have good anthropometric nutritional status at baseline, which rules out the comment by Oelofse *et al*. (2003:399-407).

Maleta *et al*. (2004:152-158) reported on an intervention study with a duration of 12 weeks amongst malnourished children aged 42 to 60 months in Malawi. One group consumed RUTF as a daily supplement, and the other group a maize-soy flour. Both groups showed a modest weight gain, with better sustaining of weight gain in the RUTF group. No effect was observed in linear growth. The researchers concluded that the use of an unfortified maize supplement instead of a fortified product could explain the negligible effect on weight gain. They also speculated that by increasing the energy density of the product with oil (which was not done) could have had additional benefit in terms of weight gain, and also that malnutrition associated illnesses could have had a negative effect on the expected weight gain of their subjects. In the present study, the HIV associated symptoms and the advanced

stage of HIV in the majority of children could have negatively impacted on the expected weight gain.

RUTF, on the other hand, was widely used with varying results in a number of intervention studies (Ciliberto *et al*., 2005:864; Ndekha *et al*., 2005:222; Nackers *et al*., 2010:407). In general, weight gain was described as average, modest or full recovery of anthropometric nutritional status. The study by Ndekha *et al*. (2005:222) included malnourished HIV-infected children as well as non-infected children. It was reported that a smaller percentage of HIV-infected than non-infected children reached full nutritional recovery (56% as opposed to 84%), and the mean time for recovery was much longer for the HIV-infected children (86 days vs. 35 days for non-infected children). The advantages of RUTF include the high energy density, long shelf life, and because it requires no cooking, it is ready to be eaten any time, several times per day. This is especially helpful in the case of young children who could eat frequent, small meals throughout the day. In the present study, the supplement was given as a replacement of the breakfast usually served in the facilities, and was only served once per day. Distributing the supplement as an addition to normal meals might have better results. On the other hand, the aim of the study was to establish whether the added α-amylase would enable the study children to eat larger quantities of the supplement.

In an intervention study by Rudolph *et al.* (2013:1-9) a fortified maize-based supplement (E'pap) was fed to children aged 36 to 72 months, regularly attending chrèches in Alexandra, Johannesburg. Children with MUAC <110 mm were not included in the study. E'pap (50 g per day) was given supplementary to the usual diet at the chrèche, twice daily and supplies for weekend feeding were taken home. No children in the study were reported HIV-infected. Although weight and height indices were evaluated, evaluation of anthropometric nutritional status and the impact of the supplement was measured using mainly bioelectrical impedance for lean body mass. A consistent increase in lean body mass was reported in the children. The researchers concluded that this product was beneficial as a supplement for malnourished persons.

In other studies similar but not identical to the present intervention study, some researchers have reported significant improvement in anthropometric nutritional status. Chinnamma and Gopaldas (1993:17,21) used a high-energy low bulk gruel (with added α-amylase to decrease viscosity) vs. a high-energy high bulk gruel complementary to the home diet (described as meagre) of Indian slum children aged 6-24 months. In their study the anthropometric nutritional status of the children improved, with significant greater benefit in the experimental group. Several other previous studies have also shown that the use of added α-amylase can increase consumption of starch-based foods (Mitra *et al*., 1995:94; Rahman *et al*., 1994:46; Moursi *et al*., 2003:249).

Although deficits in height can be reversed with proper nutrition (Bobat *et al*., 2001:209; Knox *et al*., 2003:S66; Gat-Yablonski *et al*., 2013:83), it is not surprising that stunting was not corrected during the intervention period of the current study, since stunting is a symptom of long term malnutrition and needs longer term nutrition intervention to be corrected. The onset of catch-up growth is dependent on several factors, of which one is weight gain. In most cases catch-up growth will only resume 1 to 3 months after a minimum of 85% weight for length has been attained and established (Walker & Golden, 1988:395-404).

Possible reasons why the current study did not lead to improved W/A status, can be that the energy intake of the children was insufficient. However, calculations based on measurements of actual consumption, showed that the median energy intake from supplements was 2540 kJ and 2553 kJ by the E- and C-group children respectively (Cox, 2005:62), which is higher than the energy intake from the usual breakfast at the facilities.

According to the findings of Researcher 3 (who was responsible for measuring supplement consumption), both the E- and C-groups consumed large amounts of the supplement (Cox, 2005:59). There was no significant difference in the actual supplement consumption of the experimental or control product. It appears that the control product, although it did not contain α-amylase to reduce viscosity, was mixed to a viscosity that was acceptable to the children, with the result that children in both the E- and C-groups could consume the full quantity of porridge without difficulty. Even though this could have a significant impact on the volume of the final meal, it does not have any impact on the total energy intake. Studies

that measure the outcome of similar products should be repeated over longer periods of time in order to measure their impact on child growth, which is a long-term variable. Also, the change in viscosity due to the added α-amylase enzyme depends on the enzyme activity. Failure to follow the correct reconstitution process, e.g. the use of boiling water instead of hot water (as stated on the packaging) can inactivate the α-amylase. Enzymes are proteins, and temperatures above 85°C will denature the protein, rendering the enzyme inactive. If water of too high temperature is used for reconstitution of the enzyme-modified product, the α-amylase will denature and will lose its ability to decrease the viscosity of the product (Enzyme essentials, 2009:Online).

5.5 SUMMARY

In summary, in the present study the intervention did not result in any significant improvement in the anthropometric nutritional status of either the E-group or the C-group.

The data on the anthropometric nutritional status of the HIV-infected children in the study demonstrated the following:

- The findings in terms of anthropometric nutritional status of the study population is in agreement with findings of other researchers that the growth of HIV-infected children is impaired, especially in terms of H/A.
- This study could not show improvement in the anthropometric nutritional status of the children in the study population.
- Although other researchers did find that the addition of α-amylase to a starchy food decreases the viscosity and increases the quantity that a child can consume at a time, the results of the present study could not support these findings.

CHAPTER 6 - CONCLUSIONS AND RECOMMENDATIONS

6.1 INTRODUCTION

The aim of this study was to measure the impact of an enzyme-modified, enriched maize-based supplement on the anthropometric nutritional status of children infected with HIV, who are cared for in institutions for HIV-infected and affected children in the Mangaung area of Bloemfontein.

This study formed part of a bigger study where other researchers evaluated the impact of the supplementation on the children's immune-, micronutrient- and health status.

6.2 CONCLUSION

A total of 155 children in care centres in the Mangaung area of Bloemfontein in the Free State Province were screened for HIV. A total of 37 of these children tested positive for the presence of HIV antibodies with the ELISA method, and were therefore included in the study. Of the 37 children originally included in the study, 29 completed the intervention. Although the small sample size limits the study, valuable information regarding the anthropometric nutritional, immune, micronutrient and health status of HIV-infected children in care centres have been gathered.

The anthropometric nutritional status at baseline supported the findings of other researchers that growth in HIV-infected children is significantly slower when compared to non-infected children. The prevalence of underweight for age in the present study (42.9%) was higher compared to that reported for healthy HIV-infected children in Cape Town (28%) (Eley *et al*., 2002:19), but lower than that of HIV-infected children with HIV-related symptoms in the Eastern Cape (50.9%) (Steenkamp *et al.,* 2004:unpublished). The weight for age status of the children in the present study was better than that of severely ill HIV-infected children in Gauteng, where 55.3% of the study population were reported to be severely underweight (Dramowski *et al*., 2011:20).

The high prevalence of stunting (E=57.1%; C=80%) in the study group was in accordance with findings of other researchers who reported that HIV-infected children are more often stunted than non-infected children. The prevalence of stunting in the present study is high in comparison to existing national data for children of unknown HIV status. BMI/A is not widely used by many researchers for the evaluation of anthropometric nutritional status of children. A high percentage of children in this study was classified as normal for BMI/A. Since BMI/A is an expression of weight relative to height, and the majority of the children were stunted, a high prevalence of normal BMI/A could be expected. In contrast, the upper arm anthropometry reflected a normal to moderate W/A status of the study group. No other studies could be found where upper arm anthropometry of HIV-infected children was evaluated to compare the results with. Also, the median WAZ of the E-group in this study showed a small, but significant increase from baseline to the end of intervention. Although this increase was statistically significant, the small sample size limits its interpretation.

The poor anthropometric nutritional status of children in care centres emphasises the detrimental effect of HIV-infection on nutritional status and also growth in young children, as well as the importance of extending community based nutrition intervention initiatives to care centres and other facilities taking care of HIV-infected and -affected children. Yet, very little information is available to show whether nutrition intervention can adequately reverse this phenomenon. The data of the intervention phase of this study did not show any significant improvement in the anthropometric nutritional status in either the E- or the C-group. However, what has been shown is that nutrition intervention contributes towards the outcome of drug treatment in patients living with HIV/ AIDS.

In other similar studies where the consumption of a product with added α-amylase was compared with the consumption of an identical product without enzyme modification, higher intakes with resulting higher energy intake and increase in weight were reported in the group consuming the enzyme-modified product (Chinnamma and Gopaldas, 1993:21). Several previous studies have also reported that the use of added α-amylase can increase consumption of starch-based foods (Mitra *et al*., 1995:949; Rahman *et al*., 1994:46-53; Moursi *et al*., 2003:249-257). The children consuming the enzyme modified supplement in the study by Chinnamma and Gopaldas (1993:21) consumed about 50 kJ/kg body weight

more than those in the control group. In the current study the total energy intake of the children was low, in addition to the fact that the children in the E-group did not consume more energy from the supplement than those in the C-group - the median energy intake from supplements in the present study was 2540 kJ and 2553 kJ by the E- and C-group children, respectively (Cox, 2005:62). Children infected with HIV have much higher energy needs when compared to their HIV-negative counterparts. Calculations show that children in the present study, despite the supplementation, did not consume more than 400 to 500 kJ/kg/day, which is much lower than current recommendations for HIV-infected children.

The researcher who was responsible for measuring supplement consumption in the current study, reported that the children in the E-group did not consume more of the product when compared to those in the C-group (Cox, 2005:59). It appears that the control product, although it did not contain α-amylase to reduce viscosity, was mixed to a viscosity that was palatable for the children, with the result that children in both the E- and C-groups could consume the full quantity of porridge without difficulty.

Children participating in the study had access to regular, balanced meals provided by the care centres that they were enrolled in. During the intervention period, breakfast was replaced by an energy dense enriched maize/soy blend, with enzyme modification and a second product identical in nutritional value but without enzyme modification. Despite the addition of the supplementary feeds, the daily energy intake of the participants was not sufficient to meet in the needs of children infected with HIV. The total energy provided in this study was insufficient to establish catch-up growth in HIV-infected children with growth failure. Although other researchers did prove that the addition of α-amylase to a starchy food has benefits in terms of growth in children, the results of this study could not confirm their findings. Several factors, e.g. portion size, total daily energy intake from supplement as well as home diet, could have played a role and need further investigation. Even though deficits in height can be reversed with proper nutrition (Bobat *et al*., 2001:209; Knox *et al*., 2003:S66; Gat-Yablonski *et al*., 2013:83), it is not surprising that in this study stunting was not reversed during the intervention period, since stunting is a symptom of long term malnutrition and needs longer term nutrition intervention to be corrected. Yet, when a child reaches a certain age it becomes almost impossible to reverse stunting. The onset of catch-

up growth is dependent on several factors, of which one is weight gain. In most cases catch-up growth will only resume one to three months after a minimum of 85% weight for length has been attained and established (Walker & Golden, 1988:395-404), which was therefore not possible in this study.

6.3 RECOMMENDATIONS

The high prevalence of malnutrition found at baseline, indicate that children infected with or affected by HIV are vulnerable and not necessarily protected from malnutrition by being a resident or being registered at a care centre. Care centres are often dependent on support (including financial support) from outside, and often do not have trained staff to assist with the planning, food purchases and budgeting that is necessary to ensure that all the children receive sufficient, balanced meals that can provide in all of their nutritional needs. It is important that children in these facilities are included in routine health and nutritional assessments and that the centres are included in initiatives that target malnutrition. HIV-infected children in care centres should receive aggressive nutrition support to make provision for their increased requirements and also to protect them from malnutrition and early disease progression. The inclusion of additional sources of energy dense supplements such as RUTF to current supplementation regimens for malnourished children may be needed to achieve catch-up growth in malnourished children.

The negative impact of HIV infection on the anthropometric nutritional status of the children emphasises the importance of nutrition intervention for these children, not only at household level but also in centres that take care of young children infected with or affected by HIV. To improve the outcome of future intervention studies, it is recommended that supplementation should rather be given daily as energy rich snacks in smaller portions several times throughout the day, additional to the usual diet rather than a meal replacement. The study should also be planned to increase the time period of intervention.

6.4 VALUE OF THE STUDY

Prior to this study, no baseline information was available in terms of the health-, immune- and anthropometric nutritional status of HIV-infected children in care centres in and around Bloemfontein. Valuable information regarding the anthropometric nutritional status of this group of children was gathered. The small sample size complicated the interpretation of results. However, the study brought the attention of the researchers to the fact that the majority of children in the institutions are affected and not infected by HIV. Seen in the light of insufficient food intake by the HIV-infected children in the centres, the nutritional and health status of the HIV-affected children in the centres should also be assessed. Poor nutrition can have long-term implications for them with respect to development, school achievement and their role in the economy once they contribute towards it. The negative effect of HIV infection on the anthropometric nutritional status of the children emphasises the importance of nutrition intervention in these children, not only at household level but also in centres that take care of young children infected with or affected by HIV. Nutrition intervention should, however, provide in the specific needs of HIV-infected children to ensure effective prevention and/or treatment of nutritional deficiencies and impaired growth. Nutrition intervention for HIV-infected children should always have as a goal to restore or maintain healthy body weight, not only to delay viral replication, but especially to ensure an overall good nutritional status. The use of supplementary foods as addition to the existing diet seem to have better results than using the supplement as a meal replacement, especially in young children who should eat small meals several times a day. Other studies have shown that the use of α-amylase to decrease the viscosity of starch-based foods has been proven to have benefits, even though this study could not confirm these findings. The use of α-amylase should, however, still be encouraged to take advantage of the benefits of improved bioavailability of nutrients in the presence of this enzyme.

REFERENCES

ADA. 2000. Position of the American Dietetic Association and Dietitians of Canada: nutrition intervention in the care of persons with human immunodeficiency virus infection. Journal of the American Dietetics Association, 100:708-717.

AIDSinfo. HIV Progression. [Online]. Available from: http://aidsinfo.nih.gov/education-materials/glossary/3387/hiv-progression [Accessed January 12th, 2013].

Arpadi SM, Cuff PA, Kotler DP, Wang J, Bamji M, Lange M, Pierson RN and Matthews DE. 2000. Growth velocity, fat free mass and energy intake are inversely related to viral load in HIV-infected children. Journal of Nutrition, 130:2498-2502.

Bailey R C, Kamenga MC, Nsuami MJ, Nieburg P and St Louis ME. 1999. Growth of children according to maternal and child HIV, immunological and disease characteristics: a prospective cohort study in Kinshasa, Democratic Republic of Congo. International Journal of Epidemiology, 28:532-540.

Baker PT, Hunt EE Jr and Sen T. 1958. The growth and interrelations of skinfolds and brachial tissues in man. American Journal of Physical Anthropology, 16:39-58.

Bartlett J. 2006. Pocket guide adult HIV/AIDS treatment: Johns Hopkins University. [Online]. Available from: http://hopkins-aids.edu/publications/pocketguide/pocketgd0106.pdf [Accessed January 12th, 2013].

Benjamin DK Jr, Miller WC, Benjamin DK, Ryder RW, Weber DJ, Walter E and McKinney RE. 2003. A comparison of height and weight velocity as a part of the composite endpoint in pediatric HIV. AIDS, 17(16):2331-2336.

Benjamin DK Jr, Hirschfeld S, Cunningham CK and McKinney RE Jr. 2004. Growth as a part of the composite endpoint in paediatric antiretroviral clinical trials. Journal of Antimicrobial Chemotherapy, 54:701-703.

Benn RT. 1971. Some mathematical properties of weight-for-height indices used as measures of adiposity. British Journal of Preventative and Social Medicine, 25:42-50.

Block G and Hartman AM. 1989. Issues in reproducibility and validity of dietary studies. American Journal of Clinical Nutrition, 50:1133-1138.

Bobat R, Coovadia H, Moodley D, Coutsoudis A and Gouws E. 2001. Growth in early childhood in a cohort of children born to HIV-1-infected women in Durban, South Africa. Annals of Tropical Paediatrics, 21:203-210.

Bradshaw, D, Schneider, M, Norman, R & Bourne, LT. 2006. Mortality patterns of chronic diseases of lifestyle in South Africa, In Chronic diseases of lifestyle in South Africa. Ed. by Steyn K, Fourie J and Temple N. Medical Research Council, Tygerberg:58-64.

Bunn J, Thindwa M and Kerac M. 2009. Features associated with underlying HIV infection in severe acute childhood malnutrition: a cross sectional study. Malawi Medical Journal, 21(3):108-112.

Callens S, Shabani N, Lusiama J, Lelo P, Kitetele F, Colebunders R, Gizlice Z, Edmonds A, van Rie A and Behets F. 2009. Mortality and associated factors after initiation of pediatric antiretroviral treatment in the Democratic Republic of the Congo. Pediatric Infectious Diseases Journal, 28:35-40.

Cant AJ, Gibb DM, Davies EG, Cale C and Gennery AR. 2003. HIV infection, in Forfar & Arneil's Textbook of Pediatrics. Ed. by McIntosh N, Helms P and Smyth R. 6th ed. Spain: Churchill Livingstone:1295-1309.

Carpenter CC, Cooper DA, Fischl MA, Gatell JM, Gazzard BG, Hammer SM, Hirsch MS, Jacobsen DM, Katzenstein DA, Montaner JS, Richman DD, Saag MS, Schechter M, Schooley RT, Thompson MA, Vella S, Yeni PG and Volberding PA. 2000. Antiretroviral therapy in

adults: updated recommendations of the International AIDS Society-USA Panel. Journal of the American Medical Association, 283(3):381-390.

Case A, Paxson C, Ableidinger J. 2004. Orphans in Africa: Parental death, poverty, and school enrollment. Demography, 41(3):483-508.

CDC (Centres for Disease Control and Prevention). 1994. 1994 Revised classification system for human iImmunodeficiency virus infection in children less than 13 years of age. Morbidity and Mortality Weekly Report, 43(RR-12):1-19.

CDC (Centers for Disease Control and Prevention). 2007. Coinfection with HIV and hepatitis C virus. [Online]. Available from: http://www.cdc.gov/hiv/resources/factsheets/coinfection.htm [Accessed March 12th, 2013].

CDC (Centers for Disease Control and Prevention). 2010. HIV transmission. [Online]. Available from: http://www.cdc.gov/hiv/resources/qa/transmission.htm [Accessed March 12th, 2013].

CDC (Centers for Disease Control and Prevention). 2011. Healthy weight. About BMI for children and teens. [Online]. Available from: http://www.cdc.gov/healthyweight/assessing/bmi/childrens_bmi/about_childrens_bmi.htm [Accessed March 12th, 2013].

Chan D and Kim P. 1998. HIV entry and its inhibition. Cell, 93(5):681-684.

Chesney MA, Ickovics JR, Chambers DB, Gifford AL, Neidig J, Zwickl B and Wu AVV. 2000. Self-reported adherence to antiretroviral medications among participants in HIV clinical trials: the AACTG adherence instruments. Patient care committee & adherence working group of the outcomes committee of the adult AIDS clinical trials group (AACTG). AIDS Care, 12(3):255-266.

Chinnamma J and Gopaldas T. 1993. Evaluation of the impact on growth of a controlled 6-month feeding trial on children fed a complementary feed of a high energy-low bulk gruel versus a high energy-high bulk gruel in addition to their habitual home diet. Journal of Tropical Paediatrics, 39: 16 -22.

Ciliberto MA, Sandige H, Ndheka MJ, Ashorn P, Briend A, Ciliberto HM, Manary M. 2005. Comparison of home-based therapy with ready-to-use therapeutic food with standard therapy in the treatment of malnourished Malawian children: a controlled, clinical effectiveness trial. American Journal of Clinical Nutrition, 81: 864-70.

Collins CL. 1988. Nutrition care in AIDS. Dietetic Currents, 15(3):1-25.

Collins & Leibbrandt. 2007. The financial impact of HIV/AIDS on poor households in South Africa. AIDS, 21(Supplement):S75-S80.

Council for Agricultural and Rural Development Office. Food Security and Nutrition Information System in Cambodia. 2011. [Online]. Available from: http://www.foodsecurity.gov.kh/conceptual-framework-malnutrition [Accessed May 3rd, 2013].

Cox CD. 2005. Supplement Consumption and energy intake of HIV+ children receiving an enzyme-modified, enriched maize supplement. Script submitted in partial fulfilment of the requirements for the degree Magister Scientae in Dietetics, Department of Human Nutrition, University of the Free State.

Cunningham A, Donaghy H, Harman A, Kim M and Turville S. 2010. Manipulation of dendritic cell function by viruses. Current Opinion in Microbiology, 13(4):524-529.

Dabis F and Ekpini ER. 2002. HIV-1/AIDS and maternal and child health in Africa. The Lancet, 359(9323):2097-104.

Dannhauser A, Bester CJ, Joubert G, Badenhorst PN, Slabber M, Badenhorst AM, Du Toit E, Barnard HC, Botha P and Nogabe L. 2000. Nutritional status of preschool children in informal settlement areas near Bloemfontein, South Africa. Public Health Nutrition, 3(3):303-312.

De Onis M and Blössner M. 1997. The World Health Organization Global Database on child growth and malnutrition. [Online]. Available from: http://www.who/nut/97.4 [Accessed October 5th, 2012].

De Onis M and Blössner M. 2003. The World Health Organization Global Database on Child Growth and Malnutrition: methodology and applications. International Journal of Epidemiology, 32:518-526.

De Onis M, Blössner M, Borghi E, Morris R and Frongillo A. 2004. Methodology for estimating regional and global trends of child malnutrition. International Journal of Epidemiology, 33:1260-1270.

De Onis M, Garza C, Victora CG, Onyango AW, Frongillo EA, Martines J. 2004. WHO Multicentre Growth Reference Study Group. The WHO Multicentre Growth Reference Study: planning, study design and methodology. Food and Nutrition Bulletin, Suppl 1:S15-26.

Den Besten L, Glatthaar II and Ijsselmuiden CB. 1998. Adding α-amylase to weaning food to increase dietary intake in children. A randomized controlled trial. Journal of Tropical Pediatrics, 44:4-7.

Department of Health. 2008. Integrated Nutrition Programme. A foundation for life. [Online]. Issue 5. Available from: www.doh.gov.za [Accessed January 12th, 2013].

Dibley MJ, Goldsby JB, Staehling NW, Trowbridge FL. 1987. Development of normalized curves for the international growth reference: historical and technical considerations. American Journal of Clinical Nutrition, 46:736-748.

Dong KR and Imai CM. 2012. Medical Nutrition Therapy for HIV and AIDS, in Krause's Food and the nutrition care process. Ed. by Mahan KL, Escott-Stump S and Raymond JL. 13th ed. St Louis, Missouri: Saunders, an imprint of Elsevier Inc:864-883.

Dramowski A, Coovadia A, Meyers T and Goga A. 2011. Identifying missed opportunities for early intervention among HIV-infected paediatric admissions at Chris Hani Baragwanath hospital, Soweto, South Africa. The Southern African Journal of HIV Medicine, December:16-21.

Egge E and Strasser S. 2005. Measuring the iImpact of targeted food assistance on HIV/AIDS-related beneficiary groups: Monitoring and evaluation indicators: Chapter 16:305-325.

Eley BS, Sive AA, Abelse L, Kossew G, Cooper M and Hussey GD. 2002. Growth and micronutrient disturbances in stable, HIV-infected children in Cape Town. Annals of Tropical Paediatrics, 22:19-23.

Enzyme Essentials. 2009. Amylase: The importance of carbohydrates. [Online]. Available from: http://www.enzymeessentials.com/HTML/amylase.html [Accessed June 8th, 2013].

Fenton M and Silverman E. 2000. Medical Nutrition Therapy for Human Immunodeficiency Virus (HIV) Infection and Acquired Immunodeficiency Syndrome (AIDS), in Krause's food, nutrition and diet therapy. Ed. By Mahan KL & Escott-Stump S. 10th ed. Philidelphia: W.B. Saunders Company: 889-911.

Fenton M and Silverman E. 2008. Medical Nutrition Therapy for Human Immunodeficiency Virus (HIV) Disease, in Krause's Food and Nutrition. Ed. By Mahan KL & Escott-Stump S. 12th ed. Philidelphia: W.B. Saunders Company: 991-1020.

Fontana M, Zuin G, Plebani A, Bastoni K and Principi N. 1999. Body Composition in HIV-infected children: relations with disease progression and survival. American Journal of Clinical Nutrition, 69:1282-1286.

Fergusson P, Chinkhumba J, Grijalva-Eternod C, Banda T, Mkangama C and Tomkins A. 2009. Nutritional recovery in HIV-infected and HIV-uninfected children with severe malnutrition. Archives of Disease in Childhood, 94(7):512-6.

Fisher B, Harvey RP and Champe PC. 2007. Lippincott's Illustrated Reviews: Microbiology (Lippincott's Illustrated Reviews Series), Hagerstown, MD: Lippincott Williams & Wilkins.

Frisancho AR. 1990. Anthropometric Standards for the Assessment of Growth and Nutritional Status. Ann Arbor, United States of America: The University of Michigan Press.

Frisancho AR. 2008. Anthropometric Standards. An interactive Nutritional Reference of Body Size and Body Composition for Children and Adults. Ann Arbor, United States of America: The University of Michigan Press.

Frisancho AR. 2008. CD-ROM. Anthropometric Standards. An interactive Nutritional Reference of Body Size and Body Composition for Children and Adults. Ann Arbor, United States of America: The University of Michigan Press.

Garrib A, Jaffar S, Knight S, Bradshaw D and Bennish ML. 2006. Rates and causes of child mortality in an area of high HIV prevalence in rural South Africa. Tropical Medicine and International Health, 11(12):1841-1848.

Garza C and de Onis M. 2004. WHO Multicentre Growth Reference Study Group. Rationale for developiong a new international growth reference. Food and Nutrition Bulletin, 25(Suppl):S5-S14.

Garza C and de Onis M. 1999. A new international growth reference for young children. American Journal of Clincal Nutrition, 70(Suppl):169S-172S.

Gat-Yablonski G, Pando R and Phillip M. 2013. Nutritional catch-up growth. World Review of Nutrition and Dietetics, 106:83-9.

Gibson, RS. 2005. Principles of Nutritional Assessment. 2nd edition. New York: Oxford University Press.

Gifford AL, Bormann JE, Shivley MJ, Wright BC, Richman DD and Bozzette SA. 2000. Predictors of self-reported adherence and plasma HIV concentrations in patients on multidrug antiretroviral regimens. Journal of Acquired Immune Deficiency Syndrome, 23:386.

Global Health Council. [Online]. Available from: www.globalhealth.org [Accessed January 20th, 2012].

Gilbert PB, McKeague IW, Eisen G, Mullins C, Guéye-Ndiaye A, Mboup S and Kanki PJ. 2003. Comparison of HIV-1 and HIV-2 infectivity from a prospective cohort study in Senegal. Statistics in Medicine, 22(4):573-593.

Goletti D, Weissman D, Jackson RW, Graham NM, Vlahov D, Klein RS, Munsiff SS, Ortona L, Cauda R and Fauci AS. 1996. Effect of Mycobacterium tuberculosis on HIV replication. Role of immune activation. Journal of Immunology, 157(3):1271-1278.

Gopaldas T and Chinnamma J. 1992. Evaluation of a controlled 6-month feeding trial on intake by infants and toddlers fed a high energy-low bulk gruel versus a high energy-high bulk gruel in addition to their habitual home diet. Journal of Tropical Paediatrics, 38: 278-283.

Gorstein J, Sullivan K, Yip R, de Onis M, Trowbridge F, Fajans P, Clugston G. 1994. Issues in the assessment of nutritional status using anthropometry. Bulletin of the World Health Organization, 72:273-283.

Govender T. Epidemiology of HIV/AIDS in South Africa. [Online]. Available from: http://en.wikipedia.org/wiki/HIV/AIDS in South Africa#cite note-22 [Accessed 15 September 2013]

Grant A. 2002. Clinical features of HIV in developing countries. Leprosy Reviews, 73:197-205.

Hamill PVV, Drizd TA, Johnson CL, Reed RB, Roche AF, Moore WM. 1979. Physical growth: National Center for Health Statistics percentiles. American Journal of Clinical Nutrition, 32:607-629.

Harrison D. 2010. An Overview of Health and Health Care in South Africa 1994 – 2010: Priorities, progress and prospects for new gains. A discussion document commissioned by the Henry J. Kaiser Family Foundation to help inform the national health leaders' retreat, Muldersdrift. [Online].
Available from: http://www.doh.gov.za [Accessed January 20th, 2013].

Heller L, Fox S, Hell KJ and Church, JA. 2000. Development of an instrument to assess nutritional risk factors for children infected with human immunodeficiency virus. Journal of the American Dietetic Association, 100(3):323-329.

Ivers LC, Chang Y, Jerome JG and Freedberg KA. 2010. Food Assistance is associated with improved body mass index, food security and attendance at clinic in an HIV program in central Haiti: a prospective observational cohort study. AIDS Research and Therapy, 7:33-40.

Joppe M. 2000. The Research Process. [Online],
Available from: http://www.ryerson.ca/mjoppe/rp.htm [Accessed January 12th, 2013].

Karim SSA, Churchyard GJ, Karim QA and Lawn SD. 2009. HIV infection and tuberculosis in South Africa: an urgent need to escalate the public health response. The Lancet [Online], 374: 921-933.
Available from: http://www.thelancet.com [Accessed March 3rd, 2013].

Kikafunda JK and Namusoke HK. 2006. Nutritional status of HIV/AIDS orphaned children in households headed by the elderly in Rakai district, South Western Uganda. [Online]. African Journal of Food, Agriculture, Nutrition and Development [Online], 6(1):1-28. Available from: http://www.ajfand.net [Accessed November 20th, 2012].

Kimani-Murage EW, Norris SA, Pettifor JM, Tollman SM, Klipstein-Grobusch K, Gomez-Olive XF, Dunger DB and Kahn K. 2011. Nutritional status and HIV in rural South African children. BMC Pediatrics [Online], 11:23.
Available from: http://www.biomedcentral.com/1471-2431/11/23 [Accessed March 3rd, 2013].

Knox TA, Zafonte-Sanders M, Fields-Gardner C, Moen K, Johansen D and Paton N. 2003. Assessment of Nutritional Status, Body Composition, and Human Immunodeficiency Virus-Associated Morphologic Changes. Clinical Infectious Diseases, 36(Suppl 2):S63-S68.

Krasovec KA, Fawzi W and Rollins N. 2009. Nutrition, HIV, and antiretroviral therapy in infants and children. Marlink RG, Teitelman ST, eds. From the Ground Up: Building Comprehensive HIV/AIDS Care Programs in Resource-limited settings. Washington, DC: Elizabeth Glaser Pediatric AIDS Foundation. [Online].
Available from: http://ftguOnline.org [Accessed April 10th, 2013]

Lee RD and Nieman DC. 2010. Nutritional Assessment. 5th Edition, McGraw Hill, New York.

Lévy JA. 1993. HIV pathogenesis and long-term survival. AIDS, 7(11):1401-1410.

Lepage P, Msellati P, Hitimana Dg, Bazubagira A, Van Goethem C, Simonon A, Karita E, Dequae-Merchadou L, Van De Perre P And Dabis F. 1996. Growth of human immunodeficiency type 1-infected and uninfected children: a prospective cohort study in Kigali, Rwanda, 1988 to 1993. Pediatric Infectious Disease Journal, 15(6):479-485.

Lochet P, Peyrière H, Lotthé A, Mauboussin JM, Delmas B and Reynes J. 2003. Long-term assessment of neuropsychiatric adverse reactions associated with efavirenz. HIV Medicine, 4(1):62-66.

London (London School of Hygiene and Tropical Medicine). 2009. The use of epidemiological tools in conflict-affected population. Open-access educational resources for policy-makers.

[Online]. Available from:
http://conflict.lshtm.ac.uk/page_125.htm#Malnutrition_Anthropometry_Z_scores
[Accessed May 13th 2013]

Lowenthal ED and Phelps R. 2009. Growth in HIV-infected children. HIV Curriculum for the Health Professional [Online], 254-276. Available from: http://www.bipai.org [Accessed January 12th, 2013]

Maas JJ, Dukers N, Krol A, van Ameijden EJ, van Leeuwen R, Roos MT, de Wolf F, Coutinho RA and Keet IP. 1998. Body mass index course in asymptomatic HIV-infected homosexual men and the predictive value of a decrease of body mass index for progression to AIDS. Journal of Acquired Immune Deficiency Syndrome and Human Retrovirology, 19(3):254-259.

McGovern SL, Caselli E, Grigorieff N, Shoichet BK (2002). A common mechanism underlying promiscuous inhibitors from virtual and high-throughput screening. Journal of Medical Chemistry, 45(8):1712-1722.

Maleta K, Virtanen SM, Espo M, Kulmala T and Ashorn P. 2003. Childhood malnutrition and its predictors in rural Malawi. Paediatric and Perinatal Epidemiology, 17:384-390.

Maleta K, Kuittinen J, Duggan MB, Briend A, Manary M, Wales J, Kulmala T and Ashorn P. 2004. Supplementary Feeding of Underweight, Stunted Malawian Children With a Ready-To-Use-Food. Journal of Pediatric Gastroenterology, 38:152-158.

Manary MJ, Ndheda MJ, Ashorn P, Maleta K and Briend, A. 2004. Home Based Therapy for severe malnutrition with ready-to-use food. Archives of Disease in Childhood, 89:557-561.

Mangili A, Murman DH, Zampini AM and Wanke CA. 2006. Nutrition and HIV infection: review of weight loss and wasting in the era of highly active antiretroviral therapy from the Nutrition for Healthy Living cohort. Clinical Infectious Diseases Journal, 42(6):836-842.

Marston B and de Cock KM. 2004. Multivitamins, nutrition, and antiretroviral therapy for HIV disease in Africa. The New England Journal of Medicine, 351(7):78-80.

Mason JB, Bailes A, Mason KE, Yambi O, Johnsson U, Hudspeth C, Hailey P, Kendle A, Brunet D and Martel P. 2004. AIDS, drought and child malnutrition in Southern Africa. Public Health Nutrition, 8(6):551-563.

McGovern SL, Caselli E, Grigorieff N and Shoichet BK. 2002. A common mechanism underlying promiscuous inhibitors from virtual and high-throughput screening. Journal of Medical Chemistry, 45(8):1712-1722.

McKinney RE Jr, Wesley J, Robertson WR and the Duke Pediatric AIDS Clinical Trials Unit. 1993. Effect of human immunodeficiency virus infection on the growth of young children. Journal of Pediatrics, 123:579-582.

Miller TL, Orav EJ, Martin SR, Cooper ER, McIntosh K and Winter HS. 1991. Malnutrition and carbohydrate malabsorption in children with vertically transmitted human immunodeficiency virus 1 iInfection. Gastroenterology, 100:1296-1302.

Miller TL, Evans SJ, Orav, EJ, Morris V, McIntosh K and Winter HS. 1993. Growth and body composition in children infected with the human immunodeficiency virus-1. American Journal of Clinical Nutrition, 57:588-592.

Miller TL. 2003. Nutritional aspects of HIV-infected children receiving highly active antiretroviral therapy. AIDS, 17(Suppl1):S130-S140.

Mishra V, Arnold F, Otieno F, Cross A and Hong R. 2005. Education and nutritional status of orphans and children of HIV-iInfected parents in Kenya. DHS Working papers.

Mitra AK, Rahman MM, Mahalanabis D, Patra FC and Wahed MA. 1995. Evaluation of an energy‐dense meal liquefied with amylase of germinated wheat in children with acute watery diarrhoea: a randomized controlled clinical trial. Nutrition Research, 15:939-951.

Montagnier L. 1999. Human Immunodeficiency Viruses (Retroviridae). Encyclopedia of Virology, 2:763-774.

Moursi M, Mbemba F and Treche S. 2003. Does the consumption of amylase-containing gruels impact on the energy intake and growth of Congolese infants? Public Health Nutrition, 6:249-258.

Moye J, Rich KC, Kalish LA, Sheon AR, Diaz C, Cooper ER, Pitt J and Handelsman E. 1996. Natural History of somatic growth in infants born to women infected by human immunodeficiency virus. The Journal of Pediatrics, 128(1):58-69.

Mungadze S. 2013. Single antiretroviral pill launched. [Online].
Available from: http://www.bdlive.co.za/national/health/2013/04/08/single-antiretroviral-pill-launched. [Accessed April 15th, 2013].

Musoke PM, Mudiope P, Barlow-Mosha LN, Ajuna P, Bagenda D, Mubiru M, Tylleskar T and Fowler MG. 2010. Growth, immune and viral responses in HIV-infected African children receiving highly active antiretroviral therapy: a prospective cohort study. BMC Pediatrics, [Online], 10:56.
Available from: http://www.biomedcentral.com [Accessed February 10th, 2013].

Ndhekha MJ, Manary MJ, Ashorn P and Briend A. 2005. Home-based therapy with ready-to-use therapeutic food is of benefit to malnourished, HIV-infected Malawian children. Acta Paediatrica, 94:222-225.

Newell M, Cortina-Borja M, Thorne C, Peckham C. 2003. Height, weight, and growth in children born to mothers with HIV-1 infection in Europe. The European Collaborative Study. Pediatrics [Online], 111(1):e52-e60.
Available from www.pediatrics.org/cgi/content/full/111/1/e52 [Accessed January 12th, 2013].

NFCS (The National Food Consumption Survey). 2000. Children aged 1-9 years, South Africa, 1999. NFCS Group. Editor: Labadarios D. Stellenbosch, South Africa.

NFCS-FB (The National Food Consumption Survey: Fortification Baseline). 2007. The Knowledge, attitude, behaviour and procurement regarding fortified foods, a measure of hunger and the anthropometric and selected micronutrient status of children aged 1 – 9 years and women of childbearing age: South Africa, 2005. Editor: Labadarios D. Stellenbosch, South Africa.

NIAID (National Institute of Allergies and Infectious Diseases). US Department of Health and Human Services. [Online].
Available from http://www.niaid.nih.gov/Pages/default.aspx [Accessed January 27th, 2013].

Norman R, Bradshaw D, Schneider M, Pieterse D, Groenewald P. 2006. Revised Burden of Disease Estimates for the Comparative Risk Factor Assessment, South Africa 2000. Methodological Note. Cape Town: South African Medical Research Council.

Oelofse A, Van Raaij JMA, Benade AJS, Dhansay MA, Tolboom JJM and Hautvast JGAJ. 2003. The effect of a micronutrient-fortified complementary food on micronutrient status, growth and development of 6- to 12-month-old disadvantaged urban South African infants. International Journal of Food Sciences and Nutrition, 54(5):399-407.

Ogden CL, Kuczmarski RJ, Flegal KM. 2002. Centers for Disease Control and Prevention 2000 growth charts for the United States: improvements to the 1977 National Center for Health Statistics version. Pediatrics, 109:45-80.

Oleske JM, Rothpletz-Puglia PM and Winter H. 1996. Historical Perspectives on the Evolution in Understanding the Importance of Nutritional Care in Pediatric HIV Infection. Journal of Nutrition, 126:2616S-2619S.

Oguntibeju O, van den Heever W, van Schalkwyk, F. 2007. The Interrelationship between nutrition and the immune system in HIV infection: A review. Pakistan Journal of Biological Sciences, 10(24):4327-4338.

Pollack H, Glasberg H, Lee E, Nirenberg A, David R, Krasinski K, Borkowsky W, Oberfield S. 1997. Impaired early growth of infants perinatally infected with human immunodeficiency virus: correlation with viral load. Journal of Pediatrics, 130:915-922.

Preidis GA, McCollum ED, Mwansambo C, Kazembe PN, Schutze GE and Kline MW. 2011. Pneumonia and malnutrition are highly predictive of mortality among African children hospitalized with human immunodeficiency virus infection or exposure in the era of antiretroviral therapy. Journal of Pediatrics, 159(3):484-9.

Rabie H, Marais BJ, Van Toorn R, Nourse P, Nel ED, Goussard P, Sellers N and Cotton MF. 2007. Important HIV-associated conditions in HIV-infected infants and children. South African Family Practise, 49(4):19-23.

Rahman MM, Islam MA, Mahalanabis D, Biswas E, Majid N and Wahed MA. 1994. Intake from an energy‐dense porridge liquefied by amylase of germinated wheat: a controlled trial in severely malnourished children during convalescence from diarrhoea. European Journal of Clinical Nutrition, 48:46-53.

Ramalho LC de Barros, Goncalves EM, de Carvalho WRG, Guerra G Jr, Centeville M, Aoki FH, Morcillo AM, Dos Santos Vilela and da Silva MTN. 2011. Abnormalities in body composition and nutritional status in HIV-infected children and adolescents on antiretroviral therapy. International Journal of STD & AIDS, 22(8):453-456.

Reeves JD and Doms RW. 2002. Human immunodeficiency virus type 2. Journal of General Virology, 83(6):1253-1265.

Rivera DM. 2012. Pediatric HIV infection. Medscape Reference Article [Online].
Available from: http://misc.medscape.com [Accessed March 4th, 2013].

Robinson CH, Lawler MR, Chenoweth WL and Garwick AE. 1986. Normal and Therapeutic Nutrition. 17th edition. New York: Macmillan Publishing Company.

Roche AF, Siervogel RM, Chumlea WC and Webb P. 1981. Grading body fatness from limited anthropometric data. American Journal of Clinical Nutrition, 34:2831-2838.

Rudolph M, Kroll F, Beery M, Marinda E, Sobiecki J, Douglas G and Orr G. 2013. A pilot study assessing the impact of a fortified supplementary food on the health and well-being of crèche children and adult TB patients in South Africa. [Online], 8(1): 1-9. Available from www.plosone.org [Accessed June 16th, 2013]

SAVACG (South African Vitamin A Consultative Group). 1996. Anthropometric, Vitamin A, iron and immunisation coverage status in children aged 6 to 71 months in South Africa, 1994. South African Medical Journal, 86: 354-357.

Saavedra JM, Henderson RA, Perman JA, Hutton N, Livingston RA and Yolken RH. 1995. Longitudinal assessment of growth in children born to mothers with human immunodeficiency virus infection. Archives of Pediatrics and Adolescent Medicine, 149:497-502.

Scherpbier HJ, Bekker V, Van Leth F, Juriaans S, Lange J and Kuijpers TW. 2006. Long-term experience with combination antiretroviral therapy that contains Nelfinavir for up to 7 years in a pediatric cohort. [Online]. E528-e536 Available from www.pediatrics.org [Accessed January 8th, 2013].

Semba RD and Tang AM. 1999. Micronutrients and the pathogenesis of human immunodeficiency virus infection. British Journal of Nutrition, 81: 181-189.

Shaw V and Lawson M. 2007. Clinical Paediatric Dietetics. Ed. Shaw V and Lawson M. 3rd edition. Blacwell Publishing: Oxford.

Shearer WT, Quinn TC, LaRussa P, Lew JF, Mofenson L, Almy A, Rich K, Handelsman E, Diaz C, Pagano M, Smeriglio V and Kalish L.A. 1997. Viral load and disease progression in infants

infected with human immunodeficiency virus type 1. The New England Journal of Medicine, 336(19):1337-1342.

Smith JA and Daniel R. 2006. Following the path of the virus: the exploitation of host DNA repair mechanisms by retroviruses. ACS Chemical Biology, 1(4):217-26.

Stevens W and Sherman G. 2009. [Online]. Approaches to Early Infant Diagnosis of HIV. Available from: http://ftguonline.org. Marlink RG, Teitelman ST, eds. From the Ground Up: Building Comprehensive HIV/AIDS Care Programs in Resource-Limited Settings. Washington, DC: Elizabeth Glaser Pediatric AIDS Foundation. [Accessed May 16th, 2013].

Statistics South Africa. 2008. Mortality and causes of death in South Africa, 2006: Findings from death notification. [Online].
Available from: http://www.statssa.gov.za/publications/P0309/P0309.3pdf [Accessed January 14th, 2012].

Statistics South Africa. 2010. Mid-year Population Estimates 2010. [Online].
Available from: http://www.statssa.gov.za/publications/P0302/P03022010.pdf [Accessed January 14th, 2012].

Statistics South Africa. 2013. Mid-year Population Estimates 2013. [Online].
Available from: http://www.statssa.gov.za/publications/P0302/P03022011.pdf [Accessed June 15th, 2012].

Steenkamp L, Dannhauser A, Walsh D, Joubert G, Veldman FJ, Van der Walt E and Cox C. 2009. Nutritional, immune, micronutrient and health status of HIV-infected children in care centres in Mangaung. South African Journal of Clinical Nutrition, 22(3):131-136.

Steenkamp L, von der Marwitz J and Giovanelli C. 2004. Nutritional status of HIV+ pre-school children in South Africa. Summary of unpublished research. [Online]. Field Exchange Issue 22, Available from: http://fex.ennOnline.net/22/nutritional.aspx [Accessed January 12th, 2013]

Tang J and Kaslow RA. 2003. The impact of host genetics on HIV infection and disease progression in the era of highly active antiretroviral therapy. AIDS, 17(Suppl4):S51-S60.

UNAIDS & WHO. 2003. A history of the HIV/AIDS epidemic with emphasis on Africa. [Online].
Available from: http://www.unaids.org [Accessed November 4th, 2012].

UNAIDS, 2010a: Global Report: Annex 1: HIV and AIDS estimates and data, 2009 and 2001. [Online].
Available from: http://www.unaids.org [Accessed November 4th, 2012].

UNAIDS, 2010b: Global Report: Chapter 2: Epidemic update**.** [Online].
Available from: http://www.unaids.org Accessed November 4th, 2012].

UNICEF. 1997. Conceptual framework for analyzing the causes of malnutrition. [Online].
Available from: http://www.unicef.org/nutrition/training [Accessed March 6th, 2013].

UNICEF, 1998. State of the World's Children. [Online].
Available from: http://www.unicef.org/sowc98/ [Accessed May 7th, 2013].

UNICEF. 2006. Africa's Orphaned and Vulnerable Generations: Children Affected by Aids. [Online].
Available from: www.unicef.org/publications [Accessed January 12th, 2012].

UNICEF. 2010. Children and AIDS. Fifth Stocktaking Report, UNICEF/UNAIDS/WHO/UNFPA. [Online].
Available from: http://www.unicef.org/publications [Accessed January 12th, 2012].

USAID. 2011. Ready-to-use therapeutic food. [Online]. Available from: http://blog.usaid.gov/2011/10/ready-to-use-therapeutic-food [Accessed January 12th, 2012].

Venkatesh KK, Lurie MN, Triche EW, De Bruyn G, Harwell JI, McGarvey ST and Gray GE. 2010. Growth in infants born to HIV-infected women in South Africa according to maternal and infant characteristics. Tropical Medicine and International Health, 15(11): 1364-1374.

Verweel G, van Rossum AM, Hartwig NG, Wolfs TF, Scherpbier HJ and de Groot R. 2002. Treatment with highly active antiretroviral therapy in human immunodeficiency virus type 1-infected children is associated with a sustained effect on growth. Pediatrics, 109(2):E25.

Villamor E, Misegades L, Fataki MR, Mbise RL, Fawzi WW. 2005. Child mortality in relation to HIV infection, nutritional status, and socio-economic background. International Journal of Epidemiology, 34:61-68.

Walker SP and Golden MHN. 1988. Growth in length of children recovering from severe malnutrition. European Journal of Clinical Nutrition, 42:395-404.

Wanke C. 2004. Pathogenesis and consequences of HIV-associated wasting. Journal of Acquired Immune Deficiency Syndrome, 37(Suppl5):S277-9.

Waterlow JC, Buzina R, Keller W, Lane JM, Nichaman MZ and Tanner JM. 1977. The presentation and use of height and weight data for comparing the nutritional status of groups of children under the age of 10 years. Bulletin of the World Health Organization, 55:489-498.

Waterlow JC (ed.). 1988. Linear Growth Retardation in Less Developed Countries. New York: Raven Press.

Webb AL, Manji K, Fawzi WW and Villamor E. 2008. Time-independent maternal and infant factors and time-dependent infant morbidities including HIV iInfection, contribute to infant growth faltering during the First 2 years of life. Journal of Tropical Pediatrics, 55(2):83-90.

Weiss RA. 1993. How does HIV cause AIDS? Science, 260(5112): 1273-1279.

Wheeler DA, Gibert C, Launer C, Muurahainen N, Elion R, Abrams D and Bartsch, G. 1998. Weight loss as a predictor of survival and disease progression in HIV infection. Journal of Acquired Immune Deficiency Syndromes and Human Retrovirology, 18(1):80-85.

WHO. 1990. Interim proposal for a WHO Staging System for HIV infection and disease. Weekly Epidemiological Record. 20 July 65(29).

WHO. 1994. An evaluation of infant growth. A summary of analysis performed in preparation for the WHO Expert Committee on physical status: The use and interpretation of anthropometry. WHO working group on infant growth. WHO Nutrition Unit, Geneva. [Online]. Availble from: http://who.int [Accessed October 5th, 2012].

WHO. 1995. Physical Status: The Use and Interpretation of Antropometry: Report of a WHO Expert Committee. Technical Report Series No. 854. World Health Organization, Geneva.

WHO. 1997. WHO global database on child growth and malnutrition. Compiled by Mercedes de Onis and Monika Blossner, Programme of Nutrition. [Online].
Availble from: http://who.int [Accessed October 5th, 2012].

WHO. 2003a. Nutrient Requirements for people living with HIV/AIDS. Report of a technical consultation, World Health Organization, Geneva, 13-15 May 2003. [Online].
Availble from: http://who.int [Accessed October 5th, 2012].

WHO. 2003b. Scaling up antiretroviral therapy in resource limited settings: treatment guidelines for a public health approach. [Online].
Availble from: http://who.int [Accessed October 5th, 2012].

WHO. 2005. Consultation on Nutrition and HIV/AIDS in Africa. Evidence, lessons, and recommendations for action – ICC, Durban, South Africa, 10-13 April 2005. [Online].
Availble from: http://who.int [Accessed December 8th, 2012].

WHO. 2006a. Antiretroviral Therapy of HIV Infection in Infants and Children in Resource-Limited Settings: Towards Universal Access. [Online].
Availble from: http://www.who.int [Accessed October 5th, 2012].

WHO. 2006b. WHO Child Growth Standards. Length/height-for-age, weight-for-age, weight-for-length, weight-for-height and body mass index-for-age. Methods and Development. [Online].
Availble from: http://www.who.int [Accessed March 16th, 2013].

WHO. 2008. Training Course on Child Growth Assessment. WHO Child Growth Standards. [Online].
Availble from: http://www.who.int [Accessed April 20th, 2013].

WHO. 2009a. Guidelines to an integrated approach to the nutritional care of HIV-infected children (6 months to 14 years). [Online].
Availble from: http://www.who.int [Accessed October 5th, 2013].

WHO. 2009b. WHO Anthroplus for Personal Computers. Manual. Software for Assessing Growth of the World's Children and Adolescents [Online].
Availble from: http://www.who.int [Accessed October 5th, 2013].

WHO. 2010a. Antiretroviral Therapy of HIV Infection in Infants and Children: Towards Universal Access. [Online].
Availble from: http://www.who.int [Accessed March 5th, 2013].

WHO. 2010b. PMTCT Strategic Vision 2010 - 2015. Preventing mother-to-child transmission of HIV to reach the UNGASS and Millenium Development Goals. Moving towards the elimination of paediatric HIV. [Online].
Availble from: http://www.who.int [Accessed March 5th, 2013].

WHO/UNAIDS/UNICEF. 2011. Global HIV/AIDS Response: Epidemic update and health sector progress towards Universal Access: Progress Report 2011. [Online].

Available from: http://www.who.int [Accessed November 4th, 2012].

World Bank. 2007. HIV/AIDS, Nutrition, and Food Security: What we can do. A synthesis of International Guidance. [Online]
Available from: http://siteresources.worldbank.org/NUTRITION/Resources [Accessed October 12th, 2012].

Zachariah R, Spiehmann M P, Harries AD and Salaniponi F M L. 2002. Moderate to severe malnutrition in patients with tuberculosis is a risk factor associated with early death. Transactions of the Royal Society of Tropical Medicine and Hygiene, 96(3):291-294.

ADDENDA

Addendum A1

UNIVERSITEIT VAN DIE VRYSTAAT
UNIVERSITY OF THE FREE STATE
YUNIVESITHI YA FREISTATA

DEPARTEMENT MENSLIKE VOEDING/DEPARTMENT OF HUMAN NUTRITION
Fakulteit Gesondheidwetenskappe/Faculty of Health Sciences

P.O.Box 339 BLOEMFONTEIN 9300 REPUBLIEK VAN SUID –AFRIKA / REPUBLIC OF SOUTH AFRICA
Tel: (051) 401 2894/(+2751) 401 2894 Faks/Fax: (051) 401 2869/ (+2751) 401 2869
E-pos/E-mail: gnmvmd@med.uovs.ac.za Interne posbus/Internal box G24

2004/04/20

Avril Snyman
Lebone Care Centre

Dear Avril

NUTRITION INTERVENTION PROJECT:2004: HIV POSITIVE CHILDREN

Our conversation on 25 March 2004 has reference. The Department of Human Nutrition, at the Free State University would appreciate it if you and the board can give the necessary permission to go ahead with above-mentioned project. The aim of the project is to determine the impact of nutrition supplementation on the nutrition, health and immune status of HIV infected children.

Parents/caretakers of all children participating would be invited to sign an informed consent before admission to the study. The study will be submitted to the Ethical Committee of the Faculty of Health Sciences at the Free State University to ensure compliance to ethical considerations and confidentiality will be ensured.

Dietitians and health personnel will monitor HIV+ children from May until November 2004 while they receive a daily fortified supplementary meal free of charge. This meal can be provided instead of the breakfast to permanent residents. Measurements will include daily evaluations on intake of the supplement; weekly weight measurements by a dietitian, monthly health screenings by a medical doctor and two blood samples (one at the start and one at the end of the study period).

The children in Lebone House would benefit from the regular screening while receiving a daily portion of high quality supplement (Both products to be used already on government tender). The cost of the supplement s the children will receive - free of charge - is approximately R1.70 per child per day. During the period the institution will save on the cost of breakfast as the supplement can be used as a replacement for breakfast. During the study period, no other form of nutrition intervention or supplementation (multivitamins) should take place.

We would need the following information as a matter of urgency:

- The number and ages of HIV tested children
- The number and ages of children not tested
- The current menu and portion sizes of food provided to children

Your urgent consideration to this matter would be appreciated. In case of queries, please contact Liana Steenkamp (cell: 082 8298418).

Thanking you.
Prof André Dannhauser

Addendum A2

UNIVERSITEIT VAN DIE VRYSTAAT
UNIVERSITY OF THE FREE STATE
YUNIVESITHI YA FREISTATA

DEPARTEMENT MENSLIKE VOEDING/DEPARTMENT OF HUMAN NUTRITION
Fakulteit Gesondheidwetenskappe/Faculty of Health Sciences

P.O. Box 339 BLOEMFONTEIN 9300
Tel. (051) 401 2894/(+2751) 401 2894
E-pos/E-mail: gnmvmd@med.uovs.ac.za

REPUBLIEK VAN SUID –AFRIKA / REPUBLIC OF SOUTH AFRICA
Faks/Fax: (051) 401 2869/ (+2751) 401 2869
Interne posbus/Internal box G24

2004/04/07

Sr Kgaile
Sunflower House

Dear Sr Kgaile

NUTRITION INTERVENTION PROJECT:2004: HIV POSITIVE CHILDREN

Our conversation on 25 March 2004 has reference. The Department of Human Nutrition, at the Free State University would appreciate it if you and the board can give the necessary permission to go ahead with above-mentioned project. The aim of the project is to determine the impact of nutrition supplementation on the nutrition, health and immune status of HIV infected children.

Parents/caretakers of all children participating would be invited to sign an informed consent before admission to the study. The study will be submitted to the Ethical Committee of the Faculty of Health Sciences at the Free State University to ensure compliance to ethical considerations and confidentiality will be ensured.

Dietitians and health personnel will monitor HIV+ children from May until November 2004 while they receive a daily fortified supplementary meal free of charge. This meal can be provided instead of the breakfast to permanent residents. Measurements will include daily evaluations on intake of the supplement; weekly weight measurements by a dietitian, monthly health screenings by a medical doctor and two blood samples (one at the start and one at the end of the study period).

The children in Sunflower House would benefit from the regular screening while receiving a daily portion of high quality supplement (Both products to be used already on government tender). The cost of the supplement s the children will receive - free of charge - is approximately R1.70 per child per day. During the period the institution will save on the cost of breakfast as the supplement can be used as a replacement for breakfast. During the study period, no other form of nutrition intervention or supplementation (multivitamins) should take place.

We would need the following information as a matter of urgency:

- The number and ages of HIV tested children
- The number and ages of children not tested
- The current menu and portion sizes of food provided to children

Your urgent consideration to this matter would be appreciated. In case of queries, please contact Liana Steenkamp (cell: 082 8298418).

Thanking you.

Prof Andrè Dannhauser

Addendum B1
Ethics committee reference number: 190/00

Toestemmingsvorm

TOESTEMMING

Hiermee verklaar ek _____wetlike voog van _____ wat huidiglik permanente/deeltydse versorging by_____ontvang, dat ek my toestemming verleen tot die deelname van _____ aan die navorsingsprojek, soos aan my verduidelik:

Ek is versoek dat _____ aan die projek deelneem wat uitgevoer word deur die Departement Menslike Voeding van die Vrystaatse Universiteit.
Die doel met die projek is om die impak van verrykte mieliepap op die voedingstatus, immuunstatus en gesondheidstatus te bepaal.
Sewentig HIV+ kinders sal vir 120 dae daagliks in die week een van twee soorte voedingsupplemente in die vorm van verrykte pap ontvang. Alhoewel elke kind slegs op een soort produk is, sal beide produkte voordele vir die kinders inhou.
Bloedmonsters sal van die kinders aan die begin en aan die einde van die projek deur ‘n mediese dokter versamel word.
Kinders sal op weeklikse basis geweeg word en maandeliks gemeet word.
Kinders sal twee keer per maand deur ‘n dokter ondersoek word.
Geeneen van die metings sal nadele vir die kinders inhou nie.
Deelname aan die projek is vrywillig en mag gestaak word, hoewel ek aangeraai is dat die kind die projek voltooi aangesien dit vir hom/haar voordelig sal wees.
Alle inligting, insluitend HIV status is vertroulik, maar resultate van die groep sal bekend gemaak word aan ander navorsers.
Vir die duur van die projek mag die deelnemers geen ander vorm van vitamien supplementasie gebruik nie, aangesien bykomende hoeveelhede nadele vir die kind mag inhou.

Ek is ten volle ingelig deur _____ aangaande bogenoemde aspekte.

My toestemming word uit vrye wil verleen en ek besef ook dat ek my toestemming te enige tyd kan herroep.

Geteken te _____ op _____ 2004.

Voog: _____Getuie: _____ .

Addendum B2

Ethics committee reference number: 190/00

Consent form

PERMISSION

I, the undersigned, _____legal guardian of _____ Who is currently in permanent/day care at_____, that I give consent that may participate in the project explained to me:

I have been asked that that _____ may participate in this project that is carried out by the Department of Human Nutrition from the Free State University. The aim with the project is to determine the impact of enriched mealiemeal on the nutritional-, immune- and health status of children.

- Seventy HIV+ children will receive one of two food supplements in the form of enriched mealiemeal for a period of 120 days. Although each child would have to use only one product for the whole period, both products would benefit the children.
- Blood samples will be collected from children at the beginning and end of the study by a medical practitioner.
- Children will be weighed every week, and measured every month.
- Children will undergo a health assessment twice per month which will be done by a medical doctor.
- None of the measurements would harm the children.
- Participation in the project is voluntary and patients may withdraw, although I was advised to let the child complete the project if possible, as it would benefit the child.
- All data would be treated confidentially, including HIV+ status, but the results of the group would be made available to other researchers.
- For the duration of the project no other form of vitamin supplementation may be given to the child, as it can be harmful, because they already receive adequate amounts.

I have been fully informed by _____ about the project.

I hereby agree voluntarily that the child can partake in the study and realize that my permission can be withdrawn at any time.

Signed at _____ on _____ 2004.

Guardian: _____Witness: _____ .

Addendum B3

Ethics committee reference number: 190/00

Consent form

TUMELLO

Nna, _____molebedi wa molao wa _____ Yeo a hlokometsweng sebakeng sa _____, ke fana ka tumello ya hore _____ a ka nka karolo projekeng eo ke e hlaloseditsweng:

- Ke kopuwe hore _____ a nke karolo projekeng ena e etswang ke lefapha la Phepo e Ntle ho tswa Univesithing ya Foreisitata.
- Maikemisetso a projeke ena ke ho sheba ditlamorao tsa phofo ya papa e matlafaditsweng, ho ho thuseng disereletsi tsa mmele le ho bophelo ba bana ka kakaretso.
- Bana ba mashome a supileng ba nang le kokwana ya HIV ba tla fuwa mofuta o le mong feela wa e mmedi ya dimatlafatsi (supplements) ka mokgwa wa papa e matlafaditsweng bakeng sa matsatsi a 120. Le ha bana ba tla be ba sebedisa mofuta o le mong feela wa dimatlafatsi (supplements) tsena, mefuta e le mmedi e tla ba le thuso ho bana.
- Madi a tla nkuwa ho bana qalong le qetellong ya dipatlisiso tsena ke ngaka.
- Boima le botelele ba bana bo tla nkuwa beke enngwe le enngwe.
- Bana ba tla hlahlojwa ha bedi kgweding ke ngaka.
- Bana ha ba ka ke ba utlwiswa bohloko ke ho hlahlojwa le ho methwa.
- Ho nka karolo projekeng ha se qobello, mme batswadi ba ka itokolla, le ha feela ke ile ka eletswa hore ho tla thusa ngwana haholo ha nka tswella pele ho fihlela qetellong.
- Ditaba kaofela tse nkuwang ngwaneng e tla ba tsa lekunutu, empa feela di tla sebediswa ke batho ba bang ba etsang dipatlisiso.
- Nakong ena ya projeke ena ngwana ha a tlameha ho sebedisa dimatlafatsi (supplements) tse ding. Di ka mo utlwisa bohloko hobane o tla be a se a fumana dimatlafatsi (supplements) tse mo lekaneng.

Ke tsebisitswe ka botlalo ke _____ ka projeke.

Ke dumela ka ntle le ho qobellwa hore ngwana a nke karolo dipatlisisong, mme ke utlwisisa hore tumello ya ka nka e hula nako e nngwe le e nngwe.

Signed _____ ka di _____ 2004.

Molebedi: _____Paki: _____ .

ADDENDUM C

WEEKLY MEASUREMENT OF WEIGHT AND CHECKING OF ARMBAND COLOUR CODING

FACILITY:……

		WEEK NUMBER and WEIGHT											
		1	2	3	5	6	7	9	10	11	13	14	15
		kg	kg	kg	kg	kg	kg	Kg	kg	kg	kg	kg	kg
Child nr. and armband check	1												
	√												
	2												
	√												
	3												
	√												
	4												
	√												
	5												
	√												
	6												
	√												
	7												
	√												
	8												
	√												
	9												
	√												
	10												
	√												
	11												
	√												
	12												
	√												
	13												
	√												
	14												
	√												
	15												
	√												
	16												
	√												
	17												
	√												
	18												
	√												
	19												
	√												

Addendum D

4-WEEKLY ANTHROPOMETRIC MEASUREMENTS

Facility:…… WEEK OF STUDY: 4 8 12

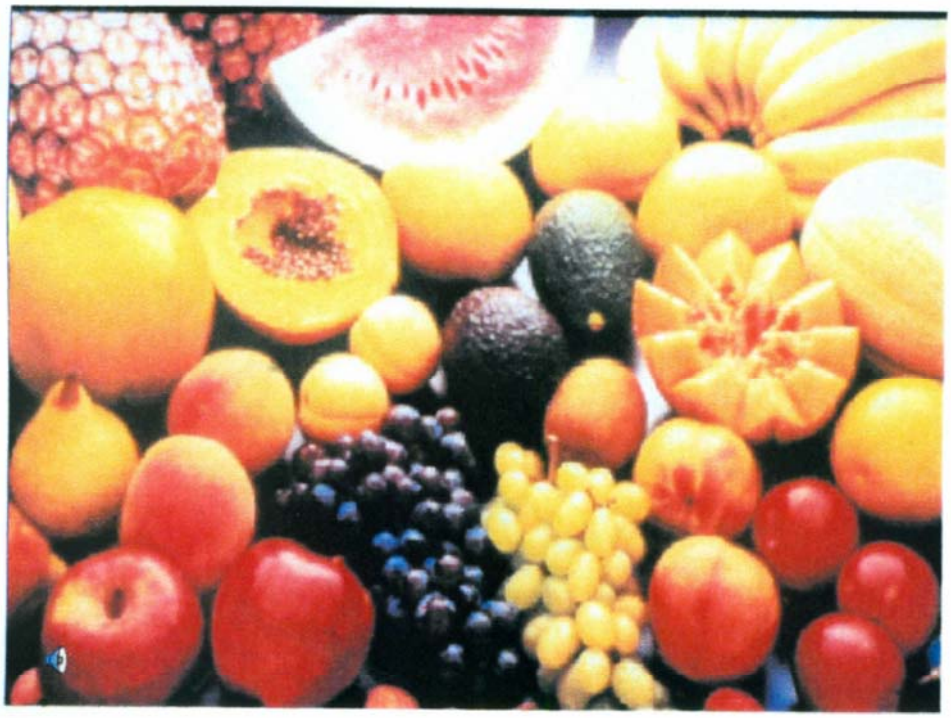
Date:……

Child name	Date of birth Yyyy/mm/dd	M/F	Weight (kg)	Height (cm)	HC (cm)	MUAC (cm)	TSF (mm) 1	 2	 3

ADDENDUM E

Training Manual for Care Centre Staff

August 2004



Index

1. The Basic Food Groups

Food can be divided into 3 basic food groups according to the role the food play in the body.

The food groups are:

- the body-building group;
- the energy group and
- the protective group.

1.1. Body-building Group

The body-building group include: meat, fish, poultry, nuts, eggs and dairy products (such as milk and cheese).

The food in the body-building group contain a substance called **protein**. Protein is the building block of the body, and helps the body to grow and to heal. Body-building foods are very important for children, because the body cannot grow without enough dietary protein. A portion body-building food, equals:

- 1 glass milk;
- 1 egg
- 30g cheese, fish, poultry or chicken (30g = matchbox size portion).

1.2. Energy Group

The energy group supplies the body with energy. Food in the energy group act like petrol for a car. a car cannot work without petrol, the body cannot function without energy foods. Foods in this gr include: **starch** and **fats**.

Starchy foods include: bread, pap, bread rolls, rice, pasta, muffins, corn, wheat and potato.

Fats include: oil, butter, margarine, cream, salad dressing, and mayonnaise.

- A portion **fat**, include: 1 teaspoon margarine /butter /oil / mayonnaise
- A portion **starchy** foods are: 1 slice bread

  ½ cup pasta, soft cooked pap

  1/3 cup rice

  ¼ cup mashed potato

1.3. Protective Group

The protective group include all types of vegetables and fruit. The protective food group contains special substances (called vitamins and minerals). Vitamins and minerals will help build the body's immune system. If the body has a good immune system, the body will be less vulnerable to certain diseases.

A portion **vegetables**: ½ cup cooked vegetables (1/2 cup cooked pumpkin)
1 cup raw vegetables (1 cup carrot salad)

A Portion **fruit**: 1 medium fruit (about the size of a tennis ball)

2. The Importance of Hygiene

Foods contaminated with harmful germs, can cause a series of harmful diseases - called **food borne diseases**. Food borne diseases include food poisoning, food infection, diarrhea and vomiting. The body can loose a lot of fluids through diarrhea and vomiting - causing dehydration. Dehydration can be very serious, and can be **fatal** in young children.

Children with **HIV infection**, have a higher risk to develop food borne diseases. Children with HIV/ AIDS have a depressed immune system, and will not recover as quickly as HIV negative children.

In order to avoid the spread of food borne disease (especially for HIV + children), the following **basic hygiene principals** should be followed:

- always wear a clean uniform/clothes while you are working with food;
- always keep your hair covered with a hairnet or hat - while you are working with food;

- always wash your hands with soap and water before working with food;
- always wash your hands with soap and water after visiting the toilet;

- cover cuts/bruises on your hands with a waterproof plaster;
- if available, wear plastic gloves when you are handling food.
- always wash fruit/vegetables thoroughly before use;
- meat/fish/chicken should be thoroughly cooked; never undercook meat.
- always use fresh food in the kitchen - a golden rule: *if in doubt, throw it out!* one should remember:
- Because children with HIV infection are at a higher risk to develop food borne diseases, left-over food should be avoided if not stored in the fridge!!

3. Mixing Instructions for supplied porridge

Two types of porridges are supplied to you. The porridge packets are colour coded; which means that the porridge in the blue packets (referred to as the BLUE PAP) are different to the porridge in the red packets (referred to as the RED PAP).The porridges should never be mixed and should always be handled apart from each other.

The porridge in the blue packets are referred to as the BLUE PAP, should be mixed in the BLUE MIXING BOWL - and served in BLUE porridge bowls to the children with the BLUE hospital armband.

The porridge in the red packets (referred to as RED PAP). should be mixed in the RED MIXING BOWL - and served in RED porridge bowls to the children with the RED hospital armband.

THE MIXING INSTRUCTIONS FOR THE PAP IS DESCRIBED IN 5 STEPS:

Step 1: weighing the pap

- Carefully weigh out the porridge - Every child should receive 150 g DRY PORRIDGE.

- Weigh the total amount of BLUE and RED PAP – the pap should be weighed apart.
- After the amount of BLUE PAP is weighed; the weighed BLUE PAP should be transferred to the BLUE mixing bowl.
- When the RED PAP is weighed, the weighed RED PAP should be transferred to RED MIXING BOWL

Step 2: mixing the pap

- After the pap is weighed, the pap can be mixed.
- For every 150g dry porridge (weighed out per child), you should add 300 ml of very hot water.
- Use boiled water, which has cooled of a bit. It is very important that VERY HOT WATER should be used.

- After the right amount of VERY HOT WATER was added to the porridge, the porridge should be mixed vigorously.

- Let the porridge stand for 5 minutes.

Step 3: Dishing up the pap

- The RED PAP should be dished up in the RED porridge bowls

- The Blue PAP should be dished up in the Blue porridge bowls.
- Every child should receive a TOTAL AMOUNT of 412 g RED or BLUE Pap

Step 4: Serving

- Serve every child with the correct amount of porridge – as mentioned in Step 3.
- It is very important that every child receives the correct porridge bowl.
- The porridge bowls are marked in order to help with identification.
- Ensure that every child receive the correct porridge bowl – according to the assigned number.
- Important: a child is only allowed to eat from his/her own porridge bowl. It is not allowed for children to share the porridge – it is not hygienic, children could cross-contaminate each other with harmful germs.

Step 5: Finishing touches!

fter the children are finished eating, clear the table. Take the bowls with left-over porridge to ıe researcher. The researcher will weigh the left over amount of porridge.

4. Completion of Spreadsheet

Value of the spreadsheet:

The spreadsheet will supply the researcher with valuable information necessary for the completion of the study.

Role of Lebone Staff:

The spreadsheet is a form that should be completed after every meal for all the children included in the study.

The fieldworker should evaluate the children's plates after every meal, and fill in a spreadsheet to help the researcher.

The spreadsheet will only consist of a few easy questions, with only **yes / no** answers.

Spreadsheet:

Date: ...28 August..... Group: ..... Group 1 : Blue Porridge.....

	Any Left-overs? Yes/ no				
Name:	Porridge	Snack	Lunch	Snack	Supper
Nancy	Yes	No	No	No	No
Maria	No	No	No	Yes	Yes

5. Importance of not taking any other supplements

During the length of the study, it is important that children should not receive ANY other forms of supplements.

"Other" types of supplements include:
multivitamins, multivitamin- syrups, e-pap, etc.

Why no other supplements?
The Blue Pap and the Red Pap contains big amounts of added vitamins and minerals. If children receive too much vitamins and minerals, it could be potentially dangerous. It is in the interest of the children that we are prohibiting the use of other supplements during the length of this study.

6. **Health Indicators Questionnaire**

Dr. Walsh is a medical practitioner who will come and examine the children on a monthly basis. It is important, however, that the children's health should be monitored on a daily basis – in order to supply the doctor with more information during the examinations.

It is requested that a questionnaire should be completed for every child on a daily basis. The questionnaire is very easy, and will only take a few minutes to complete.

If a child is ill, you must mark/tick the specific symptom on the spreadsheet – on the specific day of the week.
If a child is given medication, just fill in the name of the medication on the questionnaire.
If a child has fever, specify the temperature – and fill in on the spreadsheet.

Addendum F

BASELINE ANTHROPOMETRIC MEASUREMENTS

Facility:……

Date:……

Child name	Date of birth Yyyy/mm/dd	M/F	Weight (kg)	Height (cm)	HC (cm)	MUAC (cm)	TSF (mm) 1	 2	 3

Addendum G

END ANTHROPOMETRIC MEASUREMENTS

Facility:……

Date:……

Child name	Date of birth Yyyy/mm/dd	M/F	Weight (kg)	Height (cm)	HC (cm)	MUAC (cm)	TSF (mm) 1	 2	 3

Health of Children: Medical examination

Name: _____

Respondent number: ☐☐☐ 1-3

Date of examination: _____ d d m m y y ☐☐☐☐☐☐ 4-9

Medication:	Yes (1)	No (2)	☐ 10
If yes, specify 1. _____			☐☐ 11-1
2. _____			☐☐ 13-1
3. _____			☐☐ 15-1
4. _____			☐☐ 17-1
Temperature _____			☐☐.☐ 19-2
Pulse rate _____			☐☐ 23-2
Respiratory tempo _____			☐☐ 26-2

1. Are any of the following visible/tangible?

Jaundice	Yes (1)	No (2)	☐ 28
Pallor pale	Yes (1)	No (2)	☐ 29
Clubbing	Yes (1)	No (2)	☐ 30
Cyanosis	Yes (1)	No (2)	☐ 31
Lymphadenopathy	Yes (1)	No (2)	☐ 32
Oedema	Yes (1)	No (2)	☐ 33
Skin rash	Yes (1)	No (2)	☐ 34
Mucosal lesions	Yes (1)	No (2)	☐ 35
Ear infection	Yes (1)	No (2)	☐ 36
Loss of appetite	Yes (1)	No (2)	☐ 37
Weakness	Yes (1)	No (2)	☐ 38
Fatigue	Yes (1)	No (2)	☐ 39

2. Are there any respiratory abnormalities?

Dyspnea	Yes (1)	No (2)	☐ 40
Tachypnea	Yes (1)	No (2)	☐ 41
Crepitations	Yes (1)	No (2)	☐ 42
Wheeze	Yes (1)	No (2)	☐ 43
TB	Yes (1)	No (2)	☐ 44

3. Is there any abdominal pathology?

Splenomegaly	Yes (1)	No (2)	☐ 45
Hepatomegaly	Yes (1)	No (2)	☐ 46
Diarrhoea	Yes (1)	No (2)	☐ 47
Vomiting	Yes (1)	No (2)	☐ 48
Oral thrush	Yes (1)	No (2)	☐ 49

SUMMARY

HIV/AIDS negatively influences the health, quality of life and nutritional status of infected individuals. The negative influence on nutritional status is even worse in children than in adults, due to children's additional needs for growth.

The aim of this study was to determine the impact of an enzyme-modified, enriched maize-based supplement on the anthropometric nutritional status of children infected with HIV, and residing in or attending day care at institutions for HIV-infected and affected children in Mangaung.

A total of 155 food secure HIV-infected children aged 1 – 10 years were screened to determine HIV status. HIV-infection was confirmed in 37 clinically stable, antiretroviral naïve children, who were included in the study sample. The study was a randomised, double blind, clinically controlled, prospective trial.

Intervention over a period of 16 weeks consisted of an experimental and control supplement given to the children in the experimental- (E) and control (C) groups respectively. Both products were enriched maize/soy blends of exactly the same nutritional value, except that α-amylase was added to the E-product. The addition of α-amylase to starchy foods decreases the viscosity of the mixed product, enabling the individual to consume larger quantities for more energy and nutritional benefit, especially in the case of young children with high nutritional needs but lack of capacity to consume large enough quantities to provide in these needs.

Twenty-nine children completed the intervention. The mean age of the 29 (E=14; C=15) at baseline was 64.1 months (SD 23.6 months). Baseline nutritional status of the children was poor. Underweight for age was identified in 42.9% of both the E- and C-groups. The median Z-score for WAZ was -1.9 for both the E- and the C-group. These findings support findings of other researchers that growth in HIV-infected children is significantly slower than in non-infected children.

A high percentage of stunting was found in both groups: 57.1% in the E-group and 80% in the C-group were stunted. The median Z-scores for HAZ were -2.3 for the E- and -2.9 for the C-group. This was in accordance with findings of other researchers who reported that HIV-infected children are more often stunted than non-infected children. The prevalence of stunting in this study is high in comparison to existing national data for children of unknown HIV status.

The poor anthropometric nutritional status in children in care centres emphasises the detrimental effect of HIV-infection on the nutritional status and growth in young children, as well as the importance of extending community based nutrition intervention initiatives to care centres and other facilities taking care of HIV-infected and HIV-affected children. Although the data of the intervention phase of this study did not show significant improvement in the anthropometrical nutritional status, other studies using a product with added α-amylase did show improvement in anthropometrical nutritional status. The practical problems experienced in the present study may have had a negative effect on the outcome of the study.

In conclusion, the high prevalence of malnutrition found at baseline, indicate that children infected with or affected by HIV are vulnerable and that being a resident or being registered at a care centre does not necessarily protect them from malnutrition. It is important that children in these facilities are included in routine health and nutritional assessments and that the centres are included in initiatives that target malnutrition. HIV-infected children in care centres should receive more aggressive nutrition support to make provision for their increased requirements and also to protect them from malnutrition and early disease progression. The inclusion of additional sources of energy dense supplements such as RUTF to current supplementation regimens for malnourished children may be needed to achieve catch-up growth in malnourished children.

malnutrition; HIV; nutrition intervention; supplementation; anthropometric nutritional status; stunting, underweight; maize/soy blends; α-amylase

OPSOMMING

HIV/VIGS het ‘n negatiewe invloed op die gesondheid, lewenskwaliteit en voedingstatus van geïnfekteerde individue. Die negatiewe invloed op voedingstatus is in kinders selfs erger as in volwassenes, as gevolg van kinders se addisionele behoeftes vir groei.

Die doel van hierdie studie was om die impak van supplementasie met ‘n ensiemgemodifiseerde mieliepapsupplement op die antropometriese voedingstatus van MIV- geïnfekteerde kinders in versorgingsentrums vir MIV-geïnfekteerde en MIV-geaffekteerde kinders in Mangaung te bepaal.

Honderd-vyf-en-vyftig kinders tussen 1 en 10 jaar oud, is getoets om HIV-status te bepaal. HIV-infeksie is bevestig in 37 kinders wat nog nooit aan anti-retrovirale middels blootgestel is nie, en die 37 kinders is ingesluit in die studie. Die studie was ‘n gerandomiseerde, dubbelblinde, klinies gekontroleerde, prospektiewe intervensie.

‘n Eksperimentele produk is aan kinders in die eksperimentele groep (E) en ‘n kontrole-produk aan kinders in die kontrolegroep (K) gegee, oor ‘n tydperk van 16 weke. Beide produkte was verrykte mielie/soja produkte wat identies was in voedingswaarde, maar die eksperimentele produk het bygevoegde α-amilase bevat. Die byvoeging van α-amilase by styselprodukte verlaag die viskositeit van die produk, wat die individu in staat stel om groter hoeveelhede te eet en gevolglik meer energie- en voedingswaarde-voordeel te put, veral in die geval van jong kinders met hoë voedingsbehoeftes maar onvermoë om groot genoeg hoeveelhede te eet om in die voedingsbehoeftes te voorsien.

Nege-en-twintig kinders het die projek voltooi. Die gemiddelde ouderdom van die 29 kinders (E=14; K=15) met aanvang van die studie was 64.1 maande (SD 23.6 maande). Die kinders se basislyn voedingstatus was swak. Ondergewig is gediagnoseer in 42.9% van beide die E- en K-groepe. Die mediaan gewig-vir-ouderdom was -1.9SD in albei groepe. Hierdie basislyn bevindings het die bevindings van ander navorsers ondersteun, nl. dat groei in HIV-geïnfekteerde kinders aansienlik stadiger is as in nie-geïnfekteerde kinders.

‘n Groot persentasie lengtegroei-inkorting is in albei groepe gevind - 57.1% van die kinders in die E-groep en 80% van die kinders in die K-groep se lengtegroei was ingekort. Die mediaan lengte-vir-ouderdom was -2.3SD vir die E- en -2.9SD vir die K-groep. Hierdie bevindings het die bevindings van ander navorsers ondersteun dat lengtegroei-inkorting meer dikwels in HIV-geïnfekteerde kinders voorkom as in nie-geïnfekteerde kinders. Die voorkoms van lengtegroei-inkorting in hierdie groep was hoog in vergelyking met bestaande nasionale data vir kinders van onbekende HIV-status.

Die swak antropometriese voedingstatus van kinders in versorgingsentrums beklemtoon die nadelige effek van HIV-infeksie op die voedingstatus en groei van jong kinders, asook die belangrikheid om gemeenskapgebaseerde voedingingtervensie-inisiatiewe na sentrums vir HIV-geïnfekteerde en –geaffekteerde kinders uit te brei. Hoewel die data verkry uit die intervensie-fase van hierdie studie nie ‘n beduidende verbetering in die antropometriese voedingstatus in enige van die E- of die K-groep kon aandui nie, het die gebruik van bygevoegde α-amilase in ander studies verbetering in antropometriese voedingstatus ondervind. Die praktiese probleme wat in hierdie studie ondervind is, kon die uitkoms van hierdie studie negatief beïnvloed.

Samevattend, die hoë voorkoms van wanvoeding in hierdie studiegroep dui daarop dat MIV-geïnfekteerde en MIV-geaffekteerde kinders kwesbaar is en dat inwoning in ‘n versorgingsentrum of bywoning van ‘n dagsentrum hulle nie, soos algemeen aanvaar, vrywaar van wanvoeding nie. Dit is belangrik dat kinders in versorgingsentrums ingesluit sal word in roetine gesondheid- en voedingassesserings en dat versorgingsentrums ingesluit word in inisiatiewe vir die voorkoming en behandeling van wanvoeding. MIV- geïnfekteerde kinders in versorgingsentrums behoort meer aggressiewe voedingondersteuning te kry om voorsiening te maak vir hul verhoogde behoeftes en om hulle teen wanvoeding en vervroegde HIV/VIGS simptome te beskerm. Die insluiting van addisionele energiedigte supplemente soos RUTF tot bestaande supplementasie-regimes vir wangevoede kinders mag nodig wees om agterstallige groei in te haal.

wanvoeding; MIV; voedingintervensie; supplementasie; antropometriese voedingstatus; groei-inkorting; ondergewig; mielie/soja mengsels; α-amilase