THE USE OF ANTHROPOMETRIC INDICES AS AN ALTERNATIVE GUIDE TO INITIATING ANTIRETROVIRAL THERAPY (ART) IN CHILDREN AT THE MILDMAY CENTRE IN UGANDA

by

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Declaration

By submitting this thesis electronically, I declare that the entirety of the work contained therein is my own, original work, that I am the owner of the copyright thereof (unless to the extent explicitly otherwise stated) and that I have not previously in its entirety or in part submitted it for obtaining any qualification.

Date: 22 December 2008

ABSTRACT

Introduction: More than half a million children worldwide die from the Human Immunodeficiency Virus (HIV) and Acquired Immunodeficiency Syndrome (AIDS) each year. In Uganda, HIV/AIDS is a major cause of infant and childhood mortality. Although the government of Uganda, through various strategies, has increased access to antiretroviral drugs (ARVs), resulting in national scaling up of accessibility to antiretroviral therapy (ART), initiation of ART in resource-limited areas remains a challenge due to constraints such as the absence of or limited number of CD4 machines and related laboratory constraints. Further scaling up of ART for children would be greatly strengthened by increased access to laboratory services for CD4 counts or the introduction of alternative indicators or guidelines for the initiation of ART.

Aim: This study therefore set out to investigate, through the analysis of retrospectively collected data, whether anthropometric indices (wasting - weight for height; underweight - weight for age; and stunting - height for age) could provide a useful alternative guide when deciding about initiation of ART in children aged 2-12 years in the absence of sophisticated clinical and laboratory support.

Methods: The study was conducted at the Mildmay Centre, an HIV/AIDS specialist centre located in Kampala, Uganda. Parameters such as the age at which children had been initiated onto ART, duration on ART, World Health Organisation (WHO) and Centre for Disease Control (CDC) disease stages at time of initiation, anthropometry at time of initiation, CD4% staging at time of initiation, support received from food aid programmes, referral to other health centres as a result of malnutrition and care-giver nutrition education/counselling were all determined retrospectively from clinical records.

Results: It was found, based on CDC (2000) growth reference charts, that of the total number of children who took part in this study *(N*=125), 98.4% were mildly wasted, 52.8% mildly underweight and 75.2% mildly stunted when they were initiated onto ART. Of the children, who had WHO disease staging documented - 40% (*N*=50), the majority - 86% (*N*=43) were in WHO disease staging II and III during initiation of ART. and 96% (*N*=48) were mildly wasted. However, the relationship between WHO disease staging and wasting, underweight, and stunting at initiation of ART in children at the Mildmay centre was not significant. The relationship between CD4% and underweight or stunted children was also not significant. It was established however, that in the absence of CD4 laboratory parameters (since CD4% is vital in the initiation

of ART in children) as is the case in resource limited areas, anthropometric indices (moderate to severe wasting, weight for height -W/H) could be used concurrently with CDC and WHO disease staging to initiate ART in children. However, it is important to note that anthropometric indices on their own cannot be used as a guide for initiating ART in children.

Conclusion: Anthropometric status alone cannot be used to accurately determine when to initiate ART in children 2-12 years.

OPSOMMING

Inleiding: Meer as ‘n half miljoen kinders wêreldwyd sterf jaarliks aan die Menslike Immuungebee Virus (MIV) en Verworwe Immuungebrek Sindroom (VIGS). In Uganda is MIV/VIGS ‘n belangrike oorsaak van baba- en kindersterftes. Hoewel die regering van Uganda toegang tot antiretrovirale middels (ARV) deur verskeie strategieë verhoog het en dit tot ‘n nasionale toename in die toegang tot antiretrovirale terapie (ART) gelei het, bly inisiëring van ART in areas met beperkte hulpbronne ‘n uitdaging as gevolg van beperkinge soos die afwesigheid **van** of beperkte aantal CD4 masjiene asook verwante laboratorium beperkinge. Verhoogde toeganklikheid van ART vir kinders sal in ‘n groot mate gesterk word deur ’n verbeterde toegang tot laboratoriumdienste vir CD4 tellings of die beskikbaarstelling van alternatiewe merkers wat kan dien as riglyn vir die inisiëring van ART.

Doel: Die doel van hierdie studie was om deur retrospektiewe analise van data vas te stel of antropometriese indekse (uittering – gewig-vir-lengte; ondergewig – gewig-vir-ouderdom; en dwerggroei – lengte-vir-ouderdom) as ’n bruikbare alternatiewe riglyn kan dien in die besluit om ART in kinders tussen die ouderdom 2-12 jaar te begin in die afwesigheid van gesofistikeerde kliniese en laboratorium dienste.

Methods: Die studie is uitgevoer by die Mildmay Sentrum, ’n MIV/VIGS spesialis sentrum in Kampala, Uganda. Parameters soos die ouderdom wanneer ART in kinders begin is, duurte van ART, Wêreld Gesondheids Organisasie (WGO) en Sentrum vir Siekte beheer (CDC) stadiëring ~~ǝ~~ [Afrikaans for ‘staging’] van siekte ten tye van inisiëring, antropometrie ten tye van inisiëring, CD4% persentasie ten tye van inisiëring, hulp ontvang van voedsel programe, verwysing na ander gesondheidsentra as gevolg van wanvoeding en die opvoedkundige vlak / voorligting van die versorger is retrospektiewelik vanuit kliniese rekords verkry.

Resultate: Gebaseer op die CDC (2000) verwysingstandaarde is gevind dat van die totale getal kinders wat aan hierdie studie deelgeneem het (N=125), 98.4% matige uittering getoon het met die aanvang van ART, 52.8% matige ondergewig en 75.2% matige dwerggroei. Daar was nie ‘n betekenisvolle verband tussen WGO siekte stadium en uittering, ondergewig en dwerggroei met aanvang van ART in kinders by die Mildmay Sentrum nie. Die verband tussen CD4% en ondergewig of dwerggroei was ook nie betekenisvol nie. Daar is egter gevind dat, in die afwesigheid van CD4 laboratorium parameters (aangesien CD4% belangrik is in die inisiëring van ART in kinders) soos gevind in areas met beperkte hulpbronne, antropometriese indekse

(matig tot ernstige uittering, gewig-vir-lengte - G/L) saam met CDC en WGO siekte stadiëring gebruik kon word om ART in kinders te inisieer. Dit is egter belangrik om daarop te let dat antropometriese indekse op hul eie nie gebruik kan word as riglyn vir die inisiëring van ART in kinders nie.

Gevolgtrekking: Antropometriese status alleen het getoon dat dit nie die inisiëring van ART in kinders akkuraat kon bepaal nie

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DEFINITION OF TERMS*

Anthropometric index: The use of weight and height in conjunction with each other or with reference to age.

Anthropometry: The use of body measurements to obtain information about nutritional status.

Height-for-age: An index used to compare a child's height with the expected value of a child of the same age of a reference population, a measure of stunting.

Malnutrition: A condition of the body brought about by inadequate or excess intake of required nutrients/malabsorption and effects of disease. Anthropometrically malnutrition can be categorized as wasting, underweight, stunting or obesity in children.

Nutritional status: The physiological state of an individual that results from the relationship between nutrient intake and requirements and from the body's ability to digest, absorb and use nutrients. Anthropometry is one of the aspects that can reflect nutritional status.

Undernourishment: The result of undernourishment, poor absorption and poor biological use of nutrients consumed.

Underweight: Low weight-for-age, a composite of stunting and wasting. Is also defined as <-2 standard deviations of the weight-for-age median value of the NCHS/WHO international reference data.

Weight-for-age (underweight): An index used to compare a child's weight with the expected value of a child of the same age of a reference population; a measure of underweight.

Weight-for-height (wasting): An index used to compare a child's weight with the expected value of a child of the same height of a reference population; a measure of wasting. Often indicates recent and severe weight loss that can be attributed to acute starvation or disease.

Z-score: Deviation of a child's anthropometric indices (e.g. Weight-for-height) from the median value from the reference population. Z scores are often used in anthropometric classification of nutritional status, especially in children.

****Source: Uganda Nutrition in HIV/AIDS Guidelines (May, 2006).***[25]

LIST OF ABBREVIATIONS

ANC:	Antenatal Care
AIDS:	Acquired Immune Deficiency Syndrome
ART:	Antiretroviral Therapy
ARV:	Antiretroviral
BMI:	Body Mass Index
CDC:	Centre for Disease Control
CD4:	Helper T cell of the immune system
CI:	Confidence Interval
DAI:	Drug Access Initiative
FAO:	Food and Agricultural Organisation
HAART:	Highly Active Antiretroviral Therapy
HIV:	Human Immunodeficiency Virus
KTRSA	Keymed Trust for the Relief of Suffering in Africa
MCH:	Maternal and Child Health
MCRC:	Mildmay Centre Research Committee
MoH:	Ministry of Health
MTCT:	Mother to Child Transmission
PMTCT:	Prevention of Mother to Child Transmission
PEM:	Protein Energy Malnutrition
PEPFAR:	Presidential Emergency Plan For AIDS Relief
PHA:	People with HIV/AIDS
PI:	Protease Inhibitors
TLC:	Total Lymphocyte Count
UDHS:	Uganda Demographic and Health Survey
UNAIDS:	United Nations Joint Program on HIV/AIDS
USAID:	United States Agency for International Development
WFP:	World Food Program
WHO:	World Health Organisation

CHAPTER 1: LITERATURE OVERVIEW

1. INTRODUCTION

1.1. BACKGROUND

The Human Immunodeficiency Virus (HIV)/Acquired Immune Deficiency Syndrome (AIDS) is the fourth major cause of mortality worldwide. Twenty years after the first clinical evidence of AIDS was reported, HIV/AIDS remains a most devastating disease, accounting for 7.7% of global mortality. Approximately 33.2 million people in the world are currently living with HIV/AIDS. Of these, 2.5 million are children under the age of 15 years, an increase of 1 million from 2001. In 2007, approximately 2.5 million people were newly infected and over 330,000 children under the age of 15 years died of HIV/AIDS.. The number of new infections continues to increase daily (up to 1500), and Sub-Saharan Africa remains the worst hit region with AIDS as the leading cause of death in the region. Up to 68% of all HIV positive children live in the Sub-Saharan Africa region.[1- 4]

Regardless of the efforts to combat the disease which have seen a substantial decline in the HIV/AIDS prevalence in Uganda, HIV/AIDS remains one of the major contributors to the disease burden in the country today. By January 2006, over 2 million Ugandans were infected with HIV/AIDS and half of these died of HIV/AIDS related illness including malnutrition.[5-7] More than half a million children die from HIV/AIDS each year [1] indicating that it is a major cause of infant and childhood mortality particularly in children under the age of five years.[8-10] Most children are infected through mother- to-child transmission (MTCT)[11] and the majority of these children are at a greater risk of malnutrition due to poor/inadequate infant feeding practices.[12]

1.2. THE SITUATION/TRENDS OF HIV/AIDS IN UGANDA

HIV/AIDS was discovered in Uganda in 1982 and the epidemic progressed and spread very fast throughout the country reaching a national prevalence of 18.3%, with some areas registering a prevalence above 30%, by the end of 1992.[13] In 2007, the national prevalence stood at 6%.[14] Overall, infections are higher in urban areas than in rural areas. Kampala district, the capital city of Uganda (where the study centre for this research is situated) is located in the central region of Uganda and by 2006 the HIV/AIDS prevalence rate there was 8%, one of the highest prevalence rates in the country. Nearly 80% of all those infected with HIV in Uganda are between the ages

of 15-45 years, the most economically productive age group.[1, 14] A survey conducted in 2004 estimated that by the year 2005, 915 400 people in Uganda - including children - were living with HIV/AIDS. The same survey reported 0.7% prevalence among children younger than 5 years of age.[6]

1.2.1. Trends in nutrition

It was during the early years of the HIV/AIDS epidemic in 1988, that the importance of nutritional support was highlighted in preventing severe malnutrition, boosting the immune response and optimizing quality of life especially in improving response to treatment..[15]

To date Uganda has taken remarkable steps in addressing HIV/AIDS, including its impact on nutritional status, by developing nutrition strategies. The role of nutrition in the context of HIV/AIDS has further resulted in the development of the *National Nutrition in HIV/AIDS Guidelines*, which highlight the importance of good nutrition in HIV/AIDS.[16]

Nutritional care packages have been developed for programmes for the prevention of mother-to-child transmission (PMTCT) and integrated into antenatal care (ANC) services, and have also been included in recently developed counselling materials e.g. Maternal and Child Health (MCH) packages. Despite this, the gap between nutritional guidelines/packages and actual practice remains wide.[3] Discussions in wider forums concluded that most of the children living with HIV/AIDS today were infected through mother-to-child transmission including infant feeding. As a result, Uganda's Ministry of Health (MoH) has devised means to further strengthen nutrition by integrating nutrition components into maternal and child care to mitigate and reduce the risk of mother to child transmission. However, the rate at which nutrition information is shared is not matched by the desired behavioural changes with regard to nutritional practices.

In addition to providing HIV/AIDS treatment care and support, Uganda has also tried to address food insecurity by providing food aid and income-generating activities, a holistic approach to managing HIV/AIDS.

1.2.2. Trends in anti retroviral (ARV) therapy in children

Worldwide 7.1 million people in low and middle income countries are currently in need of ART, with only 2.015 million accessing the drugs. Across sub-Saharan Africa, UNAIDS/WHO estimated that 1.38 million people (28%) of those in need of ARVs were accessing treatment by December 2006.[2] In Uganda by February 2008, approximately half of the people in need of ARVs were receiving them i.e. 110,000 with 1,000 patients being initiated onto ART each month.[49]

Continuous scaling up of accessibility to antiretroviral therapy (ART) has created hope for people living with HIV/AIDS, including children. In 2002, only 2% of all patients receiving ARVs were believed to be children.[3] However, it remains difficult to initiate ART and monitor patient progress in resource-limited areas. The World Health Organisation (WHO) recognises the importance of laboratory monitoring for efficacy, as well as the safety of the people living with HIV/AIDS and taking the ARVs, but emphasizes that poor and restricted infrastructure should not create undue limitations or hinder ART scale-up efforts.[18]

Highly Active Antiretroviral Therapy (HAART) is a regimen that reduces viral replication and is widely available at a low cost in Uganda today. HAART is given to children to slow disease progression and improve quality of life.[17] Initiation of ART is based on various medical criteria (e.g. CD4% in children), clinical and social criteria (potential to adhere and understand the implications of poor adherence, need for treatment support) among others. ARVs do not destroy the HIV, but reduce the viral load and significantly affect the disease progression of HIV/AIDS.

Currently in Uganda the comprehensive management of HIV/AIDS includes ART[17] which is available in some government hospitals/health facilities and in the private health sector. The opportunities and treatment regimens for ART in children are multiple and are initiated in the infant stage, the latter mainly targeted through country wide PMTCT programmes. The government of Uganda is continuously encouraging families to take children in their care for HIV/AIDS counselling and testing as a strategy to identify children in need of treatment.

The goals for treating children with ARV drugs especially in sub-Saharan Africa include:

- Prolonging the survival of HIV-infected children;[17]
- Promoting optimal growth and development;
- Reducing vulnerability to infection and enhancing the immune system[19, 20], and
- Improving quality of life and delaying disease progression

Nutrition and ART enhance quality of life in the following ways:

- By lowering the viral load of the person(s) living with HIV/AIDS, ARVs improve the immune system and reduce the likelihood of opportunistic infections, resulting in improved nutritional status[7, 20];
- Drug and food/nutrition interactions play a role in the efficacy of the medication, nutrient utilisation, nutrient absorption, nutrient metabolism and adherence to ARVs, and are vital for achieving the goal of improved nutritional status[20].

1.2.3. Initiation of ART in children

At the Mildmay Centre in Kampala, Uganda – the study centre for this research - national ART treatment guidelines are used in the initiation of ART in children. Treatment is usually initiated following assessments that consider medical, clinical (including CD4 laboratory parameters), psychological and related social factors. It is general practice for healthcare facilities and hospitals that provide ARVs to take time to prepare the child/child's caregiver for ART in order to improve treatment outcomes, especially adherence.

Nutrition assessment is important during ART initiation as adequate nutritional status and household food security are two factors known to improve treatment adherence.[16] Table 1.1 indicates the WHO laboratory parameters used for ART initiation in children >18 months to < 5 years old.

WHO recommendations for initiating children older than 18 months of age on ART include:

- WHO stage 3 or 4, irrespective of total lymphocyte count (TLC)
- WHO stage 2 if TLC < 2,300 cells/mm³ if age 18 months to 6 years, or if over 6 years, TLC < 1,200 cells/mm³

- Age specific recommendations for initiation of ART in children are: children 18 months to 5 years CD4% <15%, children ≥ 5 yrs CD4% <10% i.e. CD4 count< 200 cells/mm³ (Table 1.1).

Table 1.1: Laboratory parameters used for ART initiation

Immunological marker	Age-specific recommendations to initiate ART		
	< 18 months	18 months-5 yrs	≥ 5 yrs
CD4 %	< 25%	< 15%	< 10%
CD4 count	<1500 cells/mm³	< 500 cells/mm³	< 200 cells/mm³

Further analysis of the WHO recommendations indicated that failure to thrive and severe wasting (< -3 SD Z score) among other factors can be used only in stage IV.

CD4 cells are a type of lymphocyte (white blood cells) sometimes called T cells that play a vital role in supporting the immune system and are destroyed by HIV. Normal CD4 cell numbers in a cubic millimeter of blood are between 500 and 1600 varying from individual to individual. CD4% is estimated by dividing the absolute CD4 count by the total lymphocyte count obtained from a full blood count. CD4 cell count/CD4% measures the number of cells, which are critical to the functioning of the immune system. CD4% has the strongest prognostic value for disease progression[4, 21]. CD4% refers to total lymphocytes e.g. when CD4% = 15%, this indicates that 15% of the lymphocytes are CD4 cells. In a healthy HIV negative individual, the CD4 count ranges from 500 to 1600 cells/mm³. In children CD4% is often used to initiate ART.

Using various strategies, the government of Uganda has increased the availability of ARVs resulting in the recent national scaling up of accessibility to ART. However, there have been constraints in initiation of ARVs in resource-limited areas, due to the absence or limited number of CD4 machines, frequent power cuts, lack of sufficient power to run available machines and frequent failure of unreliable machines. In order to address these challenges, a mechanism of inter-regional health facility referrals is often adopted.

1.3. IMPACT OF HIV/AIDS

Morbidity and mortality related to HIV/AIDS have affected development initiatives at individual, household, community, national and international levels. HIV/AIDS is the fourth leading cause of mortality in children under the age of 5 years. HIV/AIDS prevalence is also highest in the reproductive and child bearing population (15-49 years) resulting in an increased number of orphans and vulnerable children.[9, 13]

HIV/AIDS is the biggest threat to development and has a profound impact on economic growth, agricultural growth, income and poverty levels. In most regions hardest hit by HIV/AIDS, especially in sub-Saharan Africa, and more so in urban areas such as Kampala, Uganda, where this study was conducted, communities are economically dependent on a small number of highly skilled personnel in public management and core social services. In the worst affected countries in sub-Saharan Africa (e.g. Zambia, Zimbabwe, South Africa), cases of HIV/AIDS mortality often occur in a setting of deteriorating public services, poor employment prospects and endemic poverty exacerbated by the HIV/AIDS pandemic and are on the increase.[1,14]

In the majority of countries, HIV/AIDS has had a direct impact on the following sectors:

- Health sector: Increased work load for health workers and an increase in drug purchases for treatment of opportunistic infections;
- Civil services: Labour and human capacity is severely affected, leading to poor productivity and labour output;
- Agriculture: A reduction in agricultural production and risks related to reduced food security.

The last 20 years have highlighted a complex bi-directional relationship between food security and HIV. Poor health and death influence household food security mainly by affecting food production and household income, placing greater strain on already limited household resources.[21]

HIV/AIDS further affects families by reducing their ability to obtain food by negatively impacting on productive labour, income and household food supplies, all of which directly affect

household food security.[23] In terms of Human Capita, the Food and Agricultural Organisation's (FAO) 2005 agriculture focus report on HIV, revealed that 16 million farmers are likely to die in the next two decades in 25 countries in sub-Saharan Africa, affecting food production and indigenous farming knowledge.[2]

In addition to the above, HIV/AIDS also affects social structures, due to the increasing number of orphans. In most African communities, the number of orphans has increased as a result of HIV/AIDS. The increase in the number of orphans without parental support means that there are more mouths to feed resulting in further household food security burdens[25], which in extreme cases has worsened the already existing problem of hunger.

The HIV/AIDS pandemic in Sub-Saharan Africa also continues to affect agricultural production and household productivity, and these aspects are becoming increasingly intertwined with food and nutrition issues affecting mainly children affected by and infected with HIV/AIDS.[26]

1.4. IMPORTANCE OF GOOD NUTRITION

HIV/AIDS intertwined with poor nutrition grossly affects nutritional status. Improved nutritional status improves HIV-related outcomes, e.g. response to treatment and quicker recovery from infection.[7, 24]

Research has shown that good nutrition supports nutritional status and the immune system, especially in HIV/AIDS. These findings established that there is a close association between nutritional status and immune system impairment; the latter mainly measured by levels of CD4 count and viral load[27]. Good nutritional status can be matched with CD4 cell count increases because the immune system is strengthened, resulting in fewer opportunistic infections.[29] Anthropometric measurements and CD4 counts have been found to be significantly lower in people who had lost weight following frequent infections. A study conducted in adults indicated that patients with a CD4 count < 200 cells/mm³ had the lowest median values for anthropometric measurements.[30]

The behavioural and attitudinal aspects of dietary intake and nutritional status among people living with HIV/AIDS on ART have been largely overlooked by researchers.[25 31] Infection, no matter how mild, has an impact on nutritional status and HIV infected children are at a higher risk of malnutrition and failure to thrive. Adequate nutrition is therefore important in children to ensure that they thrive and have sufficient energy and nutrients to support the immune system.

1.4.1. Nutritional assessment in children

Nutrition management for people living with HIV/AIDS often includes nutrition assessments especially anthropometric assessment in children. Anthropometric assessments are included in the recommendations for HIV/AIDS care and management. Routine anthropometry has been one of the key indicators, used continuously to identify children at increased risk of rapid progression to AIDS and for monitoring of ART[3] outcomes.

The most commonly used anthropometric indices in children are weight for age (measure of underweight), weight for height (measure of wasting) and height for age (measure of stunting), with weight being fundamental for measuring nutritional status, since weight is affected more than height during acute infection[18]. A further advantage is that weight can be evaluated in two ways, weight for age and weight for height – the former is considered the best indicator for disease progression and survival[31]. Wasting is a measure of short term changes that could affect nutritional status such as illness/infection or inadequate food intake and will show current nutritional status. Stunting is a nutritional index that measures long term effects on nutritional status.

1.4.2. Malnutrition and HIV: A vicious cycle

It has long been recognised that synergistic interactions between infection, nutritional status and immune function can reduce dietary intake, hinder nutrient absorption, alter metabolism and consequently increase nutrient requirements leading to malnutrition, which is known to alter host defense mechanisms and accelerate disease progression.[33 -35]

Malnutrition is a condition caused by deficient or excess energy/nutrient intake or by an imbalance of nutrients and remains a fundamental problem in developing countries being linked

to mortality and morbidity.[18, 36, 37] Uganda's national HIV/AIDS nutrition guidelines indicate that nutrition and HIV/AIDS are strongly interrelated forming a vicious cycle[7, 16] (Figure 1.1).

Figure 1.1 shows that HIV/AIDS impairs the body's immune system, in turn increasing the body's vulnerability to infection. In response to HIV infection and opportunistic infections, the body's energy and nutrient requirements are increased; food intake is reduced through loss of appetite and impaired absorption of nutrients. This could subsequently lead to poor nutrition, further suppressing the immune system and strengthening the vicious cycle between malnutrition and HIV/AIDS.[33, 38]

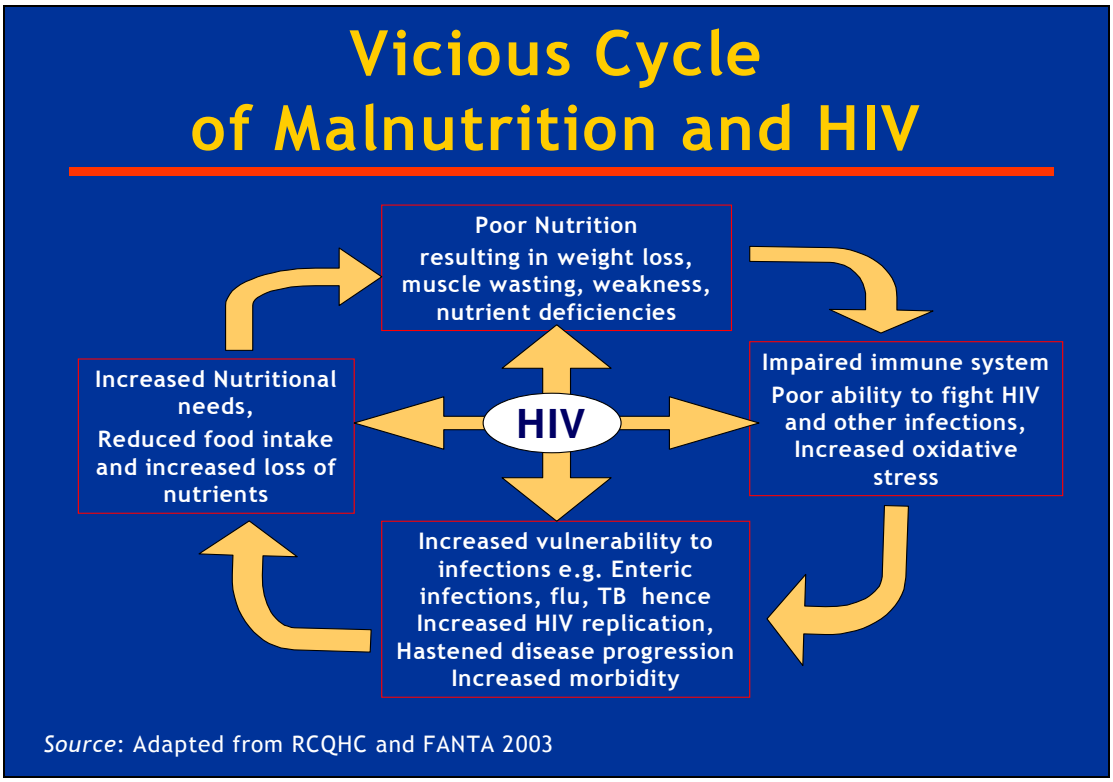

Figure 1.1: The vicious cycle of malnutrition and HIV. [7, 25]

Infection can further affect nutritional status because fatigue and decreased productivity have a direct impact on a household's ability to access food and prepare nutritionally adequate meals. This also affects care and support of household members, especially children. Malnutrition in HIV/AIDS can further be worsened by other factors such as poor dietary and nutritional practices especially for children in child-headed households.[34, 39]

The vicious cycle (Figure 1.1) confirms that managing nutrition-related complications of HIV infection and the multiple aspects of disease initiated by HIV infection, remains a challenge for those involved with HIV/AIDS prevention, care, and treatment.[40, 41]

1.4.3. Link between nutritional status and CD4 count

At least 90% of HIV infected children are affected by malnutrition.[20, 36] HIV/AIDS is associated with malnutrition and failure to thrive (Figure 1.1) because of recurrent infections and increased energy needs. Infection affects nutritional status and both (infection and nutritional status) in turn affect CD4 cells. CD4 cells are destroyed by HIV/AIDS and thus need to be built (replaced) in order to fight infection, a process which can be hindered by poor nutritional status. The more CD4 cells are destroyed by HIV, the more the immune system is impaired and the higher the chances of opportunistic infections, increasing chances of malnutrition.[43] (Figure 1.2)

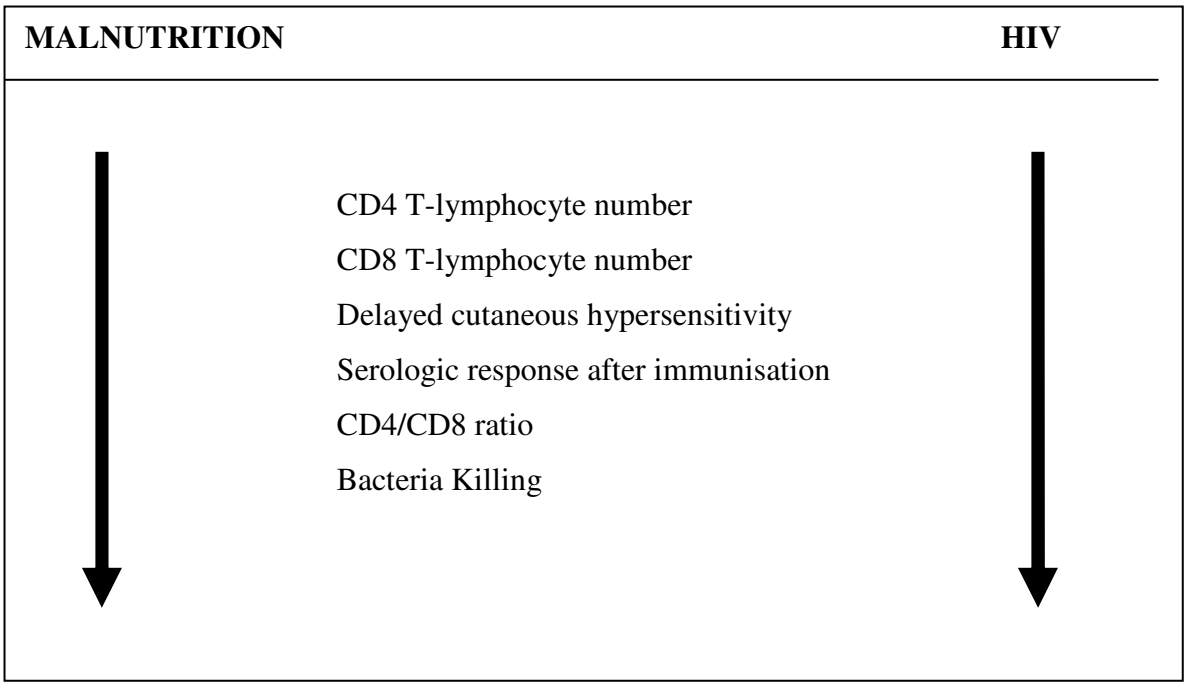

Figure 1.2: The effects of HIV/AIDS and malnutrition on the immune system. [43]

1.5. MOTIVATION FOR THE PRESENT STUDY

The World Health Organisation (WHO) strongly encourages the development of tests/tools applicable in resource-limited settings, since their availability is critical in the development of improved recommendations for the initiation of ART in children[18]. In many resource-limited

settings such as hospitals/health facilities in Uganda, CD4 count equipment is unavailable. However, further scaling up of ART programmes in children would greatly benefit from increased access to CD4 counts or the introduction of alternative markers.[3] This study therefore set out to investigate the use of anthropometric indices through analysis of retrospectively collected data as an alternative indicator for initiating ART in children at the Mildmay Centre in Kampala, Uganda,

1.5.1. Justification

There is currently limited available information in Uganda regarding the use of anthropometric indices to initiate ART especially in children. Most studies have shown that as CD4 counts decrease, the patient's nutritional status, commonly measured by anthropometry, is affected. However, published studies have mainly been conducted on adults and more investigation is required on children.

As previously mentioned (section 1.2.2), the government of Uganda has increased access to ARVs resulting in national scaling up of accessibility to ART, creating hope for many people including children living with HIV/AIDS.. However, initiation of ART in resource-limited areas remains a challenge due to the absence or limited availability of CD4 equipment, and related laboratory constraints. Even when equipment is available, there are frequent power cuts and, children are often referred to other health centres with the occasional inter-district referral being made to enable CD4 counts to be determined before initiation onto ART.

If a strong correlation between anthropometric indices and CD4% is confirmed, and if the study finds that anthropometric indices can be used as an alternative guide to initiate ART, the results of this research study would support the following statement: "*In the absence of sophisticated clinical and laboratory support, anthropometry may also prove a useful guide for deciding when to initiate antiretroviral therapy in children*".[4]

CHAPTER 2: METHODOLOGY

2. METHODOLOGY

2.1. RESEARCH AIM

The purpose of this study was to investigate the use of anthropometric indices as an alternative guide to initiating ART in children aged 2-12 years at The Mildmay Centre, Kampala, Uganda.

2.2. RESEARCH OBJECTIVES

The objectives of this research were therefore to:

- Investigate the relationship between anthropometric indices (weight for height - wasting, weight for age – underweight, height for age - stunting)) and CD4% counts at the time of initiating ART in children aged 2-12 years at the Mildmay Centre, Kampala, Uganda.
- Identify the anthropometric index (ices) with the strongest correlation with CD4% counts when initiating ART in children aged 2-12 years at the Mildmay Centre, Kampala, Uganda.
- Describe the trends in anthropometric indices as predictors of CD4% count changes in children aged 2-12 years attending the Mildmay Centre, Kampala, Uganda.

2.3. STUDY DESIGN OVERVIEW

The study domain was mainly quantitative and was designed as an analytical retrospective study using longitudinally collected data from the children's medical records stored in the Mildmay Centre data bank. The children's medical records contained information on parameters such as anthropometric measurements e.g. weight and height on each visit, CD4% counts, age, social background and treatment/medical history.

2.3.1. Study site

The Mildmay Centre is an HIV/AIDS specialist centre located in Kampala, Uganda, providing care, treatment and training in HIV/AIDS. The centre provides treatment and care for patients enrolled on ART and patients not on ART, but receiving regular treatment for opportunistic infections. The centre has been operational since 1998. By 2006 (at the time the data was collected), it had treated more than 11,000 people with HIV/AIDS (some on ART and others in care). Of the 11,000 patients, 5,700 were still regularly seeking treatment at the centre with

children (2-18 years of age) comprising just over half (N = 2,900) of the centre's clients, 650 of whom were on ART and 350 of them aged from 2-12 years.

The Centre offers a holistic approach to the treatment and care of people living with HIV/AIDS and the services offered include comprehensive medical care, social support, voluntary counselling/testing, community outreach programmes and spiritual care. Social support for children includes the provision of scholastic material, school fees and shelter (through referral) for child-headed households. The Mildmay Centre runs four clinics weekly and clinics are accessed only by people living with HIV/AIDS (adults and children).

The staff at the centre comprises medical officers, clinical officers, nurses, physicians, social workers, pediatricians, a nutritionist, counselors, pharmacists, laboratory technicians, physiotherapists, a radiographer, an occupational therapist, spiritual counselors, medical records staff, monitoring/evaluation staff, administration staff and volunteers.

Nutritional care and support, with a food aid component as an intervention to address household food insecurity, is one of the services provided at the Mildmay Centre through the nutrition department. The food aid programme was started because of observations and studies that have shown that nutrition counseling alone cannot stimulate increased energy intake in extremely food insecure people living with HIV/AIDS[3, 44]. At the time of this study, food aid was being provided through the World Food Program (WFP) and United States Agency for International Development (USAID) Food for Peace Program. Following household food security assessment, a select number of patients were provided with a food ration consisting of corn soya blend, beans/peas, maize flour and vegetable oil on a monthly basis.

The services at the Mildmay Centre are supported by national and international organizations including USAID, private donors, government organisations (Uganda's Ministry of Health) and the Centre for Disease Control (CDC). The largest funding for ART is obtained from the Presidential Emergency Plan for AIDS Relief (PEPFAR), a United States of America (USA) government funded programme.

2.4. STUDY POPULATION

Details of the sample selection for this study and the resultant sample size respectively are provided in sections 2.4.1 and 2.4.2

2.4.1. Sample selection

The study population comprised children on ART of not less than 2 years and not more that 13 years of age (children 12 years 4 months or 12 years 9 months were included) who regularly attended clinics at the Mildmay Center. The sample size was selected from the available medical records database and based on the inclusion and exclusion criteria listed below.

Inclusion criteria:

- Children initiated onto ART from the Mildmay Centre and not at any other health treatment facility.
- Children of not less than 2 and not more than 13 years of age on ART (i.e. a child 12 years and 4 months or 12 years 9 months would be included in this study).
- Children with records of height taken on each visit or at 4-month intervals and weight taken and recorded on each visit.
- Children reported to be adhering well to the ART as indicated in the child's medical file. (Adherence based on pill count and percentage calculated. Adherence is supposed to be 100%, however 95%- 97% was considered acceptable by the Mildmay Centre at the time, in special circumstances only.)
- Children who had CD4% measured to monitor effects of treatment.

Exclusion criteria

- Children whose records were missing the anthropometry measurements (height and/or weight) at initiation onto ART.
- Children whose records were missing the laboratory data (CD4%/count) at initiation of ART and/or when the child was reviewed at 4-6 months intervals.
- Children less than 2 years and more than 13 years of age on ART (i.e. a child that was 13 years and 1 month or 13 years 4 months was excluded from this study)

- Treatment defaulters/poor adherence to treatment (adherence less that 95% based on pill count),
- Children who had just started ART (been on treatment for less than 3 months) and as a result did not have much documentation on file or and had not been followed up as required.
- Children who had their ART treatment initiated from another treatment centre.

2.4.2. Sample size

Sample size was determined from the available medical records database and included an inbuilt mechanism for taking samples in small populations[45], the details of which are provided in Appendix 1. Using this method, 186 randomly selected children of the 350 children aged between 2-12 years of age who were on ART, provided a representative sample.

All the file numbers of the 350 children were accurately recorded and placed in a box from which 186 of them were randomly picked, representing the files from which data for use in this study would be collected. However, on closer inspection of the files, 61 of the children had to be excluded as a result of missing data (see exclusion criteria above) reducing the sample size to 125. It is important to note however that because sampling had to remain random (and not stratified), none of the remaining 164 patient files (those not originally picked) could be selected for inclusion in the sample because this would imply that the investigator would have created bias by looking for files with completed data and the sample selection exercise would no longer be random/applicable.

2.5. DATA COLLECTION

2.5.1. Medical records/ logistical considerations

Data were captured from each of the 125 children's medical files and entered into a pre-designed data collection tool (Appendix 2). The data collection tool allowed gathering of data on the following:

- Socioeconomic variables (area of residence, date the child started attending the clinic)
- Medical history (duration on ART, CD4% at initiation of ART and CD4 count monitoring)

- Disease staging criteria (WHO and CDC disease stages)
- Anthropometry (weight and height before/after initiation of ART, weight and height during subsequent follow up visits)
- Programmes providing ART support for the child.
- Nutritional support/interventions (nutrition education and counseling, referral for management of malnutrition)
- Food aid support
- CD4 count and CD4% on subsequent clinical visits.
- Weight trends during subsequent clinical visits.

The above data were collected by the investigator with the assistance of three data collectors. The data collectors were university graduates working at the Mildmay Centre and provided social support to the Centre at the time. The data collectors had gained experience in working in the medical department managing the Mildmay Centre. Prior to data collection, the investigator conducted a two day training exercise during which the data collectors were educated on issues relating to patient confidentiality and ethics in addition to the following:

- A general overview of the study, the objective of data collection and the use of the data collection tool.
- How to access medical files from the medical records which had been randomly picked.
- Accurate capturing of data from the files into the data collection tool, (a pilot data collection exercise had been conducted to test the efficacy of the questionnaire as a research instrument).

In the pilot exercise referred to above, the data collection tool was sent to the Mildmay Centre Research Committee (MCRC) as a centre protocol requirement. The MCRC team provided input based on what the investigator had proposed to study. Using inactive records (records of children who had died or were no longer receiving services at the Mildmay Centre), trained data collectors used the data collections system demonstrated during training to retrieve records and fill the data collection tool. Each data collector accessed 10 files as per the inclusion and exclusion criteria and filled the tool. The completed tools were checked by the investigator and related issues

which arose were addressed prior to the data collectors proceeding to collect data used in this study.

Collected data were verified by the investigator who randomly cross checked the filled tool against the files. The investigator ensured that all tools were fully completed before data from the tools were entered into an appropriately developed computer programme by the statistician and his team. The statistician employed two people to enter the data into the computer programme, and cross checked the two entries using the most accurately entered data. Data collectors were regularly supervised by an intern nutritionist and the investigator and all data collected were entered into a system designed by the statistician before going under "cleaning" (checking and verification) by a data analyst and the investigator. The data were sent to the University of Stellenbosch statistician who verified the final results as recorded in the relevant section of this thesis.

2.5.2. Quality control

- Reliable and valid data capturing tools were designed. The tool was tested at various stages to ensure that any data needed was not overlooked. The tool was pre-tested using volunteers who randomly accessed files that were no longer in use e.g. records of children who had passed away and were no longer in the record department's active system or adults' medical files.
- As previously indicated in section 2.5.1 above, all data collectors involved in this study underwent a two-day training exercise conducted by the investigator at the Mildmay Centre, Kampala, Uganda. The training exercise covered topics such as data collection strategies and techniques in order to enhance/improve data collection skills. During the training course, a pilot data collection exercise was conducted under the supervision of the investigator to ensure that all data collectors had learnt the procedures and understood the task at hand.
- During data collection, completed data capturing tool records were randomly cross-checked against file records by the intern nutritionist and the investigator to avoid errors and to ensure that the correct data from the medical files had been captured. Completed tools were also randomly checked for uniformity and accuracy of the captured data once again before filing.

- Random spot checks were conducted by the investigator and occasionally the intern nutritionist to ensure that data collectors were adhering to the correct procedures during the exercise e.g. verifying if the data collector had retrieved the correct medical file.
- A statistical check for errors was conducted by having two different data collectors independently enter the same set of data into two separate systems, a checking mechanism designed by the statistician. These systems were both checked for consistency, and any errors corrected.
- Particular monitoring of data collection, entry, recording and analysis was a continuous process undertaken by the investigator throughout the duration of the research process.
- Data were sent to the appointed statistician for verification of results based on these data.

2.5.3. Procedures used for anthropometry measurements and CD4%

2.5.3.1. Anthropometry measurements

Anthropometry measurements (height and weight) of children at the Mildmay Centre were taken using standardised equipment when the children were dressed in light clothing and without shoes. Height measurements were taken using WHO approved SECA stadiometers while weight was measured using a SECA Salter digital weighing scale (manufactured in Australia). Anthropometry was measured by nurses/centre volunteers specifically trained in recording anthropometric measurements (training enhanced at centre). For quality control, anthropometry measurement techniques were occasionally conducted under the supervision of the nutritionist and/or nursing department supervisor.

The following procedure was followed when taking measurements of height in children:

- Children removed shoes and any heavy clothing to avoid interference with measurements.
- The child stood directly below the stadiometer (permanently fixed to a straight wall in the triage/reception area at the Mildmay centre). Feet were placed together, ensuring that they touched the base of the wall and legs straightened.
- The child was asked to look straight forward, keeping his/her head level with the ground.
- The height reading was taken and the value recorded to one decimal place in centimeters (cm) in the child's medical file.

The following procedure was applied during weight measurements in children:

- The weighing scale was calibrated and set at the zero kg mark.
- Dressed in minimal clothing and without shoes, the child stood unsupported on the weighing scale.
- The weight value was read and recorded in the child's medical file to one decimal point in kilograms (kg).

2.5.3.2. CD4% counts

CD4% was analyzed in a well equipped laboratory at the Mildmay Centre and the results of laboratory investigations documented in the child's medical file. All laboratory procedures and investigations were conducted as per regulations of the Mildmay Centre and Uganda's Ministry of Health (MoH), CDC and WHO. Staff in the laboratory regularly attend refresher training courses and are consistently updated (continuous medical education) on aspects related to laboratory procedures and investigations.

Quality control was ensured at three different levels: pre-analytical, analytical and post analytical. During the pre-analytical level, it was ensured that the sample was collected correctly, labelled accurately, delivered to the laboratory promptly and stored safely. Blood samples were drawn from the child and placed in appropriate laboratory specimen containers and were analysed within a day of collection. The samples were stained and laboratory procedures such as 'full blood' were conducted, using an automated machine and adding a variety of chemicals to the sample depending on the parameter under investigation..

At the analytical level, staff in the laboratory ensured that reagents were well prepared. . Machine controls were checked each day to ensure that the machine was operating well. The CD4 machine used at the Mildmay centre at the time of study was the Florescence activated cell sorter, Model: Facs caliber, Make: Becton Dickson, BD; a sophisticated machine capable of sensitive measurements.

In the post analytical level, results were interpreted and reported accurately as a mechanism to enable medical treatment decisions., Regular supervision was conducted by the laboratory manager to avoid transcription errors in medical files.

2.6. DATA ANALYSIS

Data were edited, coded, classified, tabulated and explored to adjust for any missing information and correcting any outliers, where applicable. Data were analysed using the Statistical Package for Social Sciences (SPSS version 10). Anthropometric data (weight and height), sex and age were analysed using the EPI–INFO (version 6) package with nutstat software. This was the preferred package for the anthropometric description of a group of children. An analysis of Z-scores was calculated, using the CDC (2000) growth reference chart. To check for significance of findings, for cross tabulations, Chi square, P-value at 95% level of confidence were used with P value >0.05 indicating no statistical difference and P value < 0.05 indicating a significant difference. Correlation coefficients were also determined at 95% and means of analysis was determined using standard deviation and averages.

2.7. ETHICS CONSIDERATION

The study protocol was submitted to the Committee for Human Research, University of Stellenbosch and approved (ref N05/11/188).

- Permission to undertake this study at the study site was sought and obtained through the Mildmay Centre Research Committee (MCRC).
- Patient confidentiality was maintained throughout the study.
- Information provided to the researcher was only used for this study, and was not shared for any other purposes or studies. MCRC permitted the access and use of the files to provide the information needed to successfully conduct this study.
- All literature material referenced in this study has been acknowledged.

CHAPTER 3: RESULTS

3. RESULTS

3.1. NUMBER AND AGE OF CHILDREN USED IN THIS STUDY

The total number of children included in this study was 125 (68 boys and 57 girls). Of these, 37.6% (*N*=47) were initiated onto ART between the ages of 2-5years, 42.4% (*N*=53) between the ages of 6-9 years and 20% (*N*=25) between the ages of 10-12 years.

3.1.1. Duration on ART

All the children included in the study were on ART for periods ranging from less than one year to more than four years (Table 3.1). All of them, however, had been on ART for more than three months. The majority of the children (74.4%) had been on ART for a period of 1-2 years at the time of the study.

Table 3.1: Duration on ART

Duration on ART (Years)	No. of children (*N*)	Percentage (%)
Less than 1	8	6.4
1 - 2	93	74.4
3 - 4	18	14.4
> 4	6	4.8
Total	125	100.0

3.1.2. Disease staging

WHO disease staging criteria

Of the total number of children who took part in this study (*N*=125), only 40% (*N*=50) had documentation indicating WHO disease staging criteria at the time ART was initiated. Of these, 10% (*N*=5), 58% (*N*=29), 28% (*N*=14), and 4% (*N*=2), started ART in WHO disease stages I, II, III and IV respectively (Table 3.2). The majority of children (86%) were initiated on ART when they were symptomatic (WHO disease stages II and III).

Table 3.2: WHO disease staging at initiation of ART

WHO Disease stage	No. of children started on ART *(N)*	Percentage (%)
I (Asymptomatic, normal activity)	5	10.0
II (Symptomatic, normal activity)	29	58.0
III (Symptomatic, bed ridden)	14	28.0
IV (Symptomatic, onset of AIDS)	2	4.0
Total	50	100.0

CDC disease staging at initiation of ART

Of the 38.4% (*N*=48) children who had CDC disease staging documentation in their files at initiation of ART, 52.1% (*N*=25) were started on ARV drugs when they were in CDC disease category A and 29.2% (*N*=14*)*, in category B (Table 3.3).

Table 3.3: CDC disease staging at initiation of ART

CDC Disease Stage	No of Children started on ART *(N)*	Percentage (%)
Category N (Not symptomatic)	1	2.1
Category A (Mildly symptomatic)	25	52.1
Category B (Moderately symptomatic)	14	29.2
Category C (Severely symptomatic)	8	16.7
Total	48	100.0

There was a similar trend between the WHO and CDC disease staging criteria during initiation of ART. Of the total number of children initiated onto ART using the CDC and WHO staging, more

than three quarters of the children (*N*=43 for WHO stages and *N*=39 CDC staging) were initiated on ART while symptomatic (WHO stages II, III) and (CDC stages A and B), (Table 3.2 and 3.3).

CD4% at initiation of ART

The majority of children 71.2% (*N*=89) were initiated onto ART based on the CD4% guideline criteria. The remainder were initiated on ART based on clinical assessments, regardless of the CD4% guideline on other national ARV initiation policies and guidelines. Of these, 80.9% (*N*=72), were initiated onto ART when CD4% was <15 %, and 19.1% (*N*=17) were initiated at the time of this study with a CD4% >15% as per the Uganda and Mildmay Centre policy and guidelines for children in this age group in resource limited areas (Table 3.4).

Table 3.4: CD4% at initiation of ART

CD4%	No of children started on ART *(N)*	Percentage (%)
≤15 %	72	80.9
> 15%	17	19.1
Total	89	100.0

3.2. ART SUPPORT PROGRAMMES/INITIATIVES

3.2.1 ART funding programmes

With funding support from the Presidential Emergency Plan For AIDS Relief (PEPFAR), the largest ART supporting programme in Uganda, 62.6% (*N*=77*)* of infected children were supported and receiving ART at the time of this study (Table 3.5).

3.2.2 Food aid support for ART beneficiaries

Of the total number of children who took part in this study (*N*=125), only 8.8% (*N*=11) were enrolled onto the food aid programmes at the Mildmay Centre and received monthly food rations (Table 3.6).

Table 3.5: ART funding support at the Mildmay Centre

ARV Provider	No. of Children on ART *(N)*	Percentage (%)
PEPFAR*	77	61.6
KTRSA*	13	10.4
Ministry of Health	11	8.8
Private/Self sponsored	16	12.8
Other	8	6.4
Total	125	100.0

* Keymed Trust for the Relief of Suffering in Africa (KTRSA), Presidential Emergency Plan For AIDS Relief (PEPFAR)

Table 3.6: Children enrolled on the Food programmes at the Mildmay centre

Enrolled on food programmes	No of children *(N)*	Percentage (%)
Yes	11	8.8
No	114	91.2
Total	125	100.0

3.2.3. Referral of children for nutrition interventions (Management of malnutrition)

Only 19 (15.2%) of the total number of children who took part in this study (*N*=125) were referred by the Mildmay Centre to other Centres/hospitals for management of malnutrition. These referrals were based on clinical judgments and assessments that identified need for management of malnutrition which the centre was not able to provide, since it is an outpatient facility. Patients needing admission were consequently referred (Table 3.7).

Table 3.7: Number of children referred to other centres for management of malnutrition

Referred for management of malnutrition	No of children *(N)*	Percentage (%)
Yes	19	15.2
No	106	84.8
Total	125	100.0

3.2.4 Nutrition education

Of the total number of children involved in this study (*N*=125), only 14.4% (*N*=18) of the children's care-givers had received comprehensive nutrition education and counselling through the nutrition department at the Mildmay Centre (Table 3.8) at the time of the study. Those who had received comprehensive nutrition education through the caregivers were clearly indicated by the nutritionist in their file records. Other children would have received nutrition education and information from nurses, counselors and clinicians, but not comprehensively, and this would not have been documented in the file as the caregiver would not have been referred to the nutritionist.

Table 3.8: Comprehensive nutrition education received by child's caregiver

Received nutrition education	No of caregivers *(N)*	Percentage *(%)*
Yes	18	14.4
No	107	85.6
Total	125	100.0

The caregivers were referred to the nutrition department at the Mildmay Centre to be educated on good nutrition in HIV/AIDS. This referral would be based on clinical assessments identifying symptoms that needed dietary interventions e.g. diarrhoea, nausea, loss of appetite and malnutrition. On the other hand, the care givers, themselves, could initiate an inquiry to the department concerning a balanced diet for the children. About 50% of caregivers referred to the nutrition department, received nutrition information on the suitability of a balanced diet (Table 3.9).

3.3. ANTHROPOMETRIC STATUS (WASTING, UNDERWEIGHT AND STUNTING) AT INITIATION OF ART

3.3.1 Wasting in children at initiation of ART

All the children who took part in this study (*N*=125) were on ART and of these, it was established that 98.4% (*N*=123) were mildly wasted [Z score > -2 Standard Deviation (SD); weight/height] and 1.6% (*N*=2) were moderately wasted (Z score < - 2SD) according to CDC (2000) growth reference charts (Table 3.10).

Table 3.9: Topics covered during nutrition counseling and education

Topic	No of caregivers *(N)*	Percentage (%)
A suitable balanced diet	9	50.0
A suitable diet for chewing/oral sores problem	1	5.6
A suitable diet for nausea/vomiting	1	5.6
A suitable diet for loss of appetite	2	11.1
Management of malnutrition	1	5.6
Dietary management of weight loss	3	16.7
Other (e.g. food aid assessment)	1	5.6
Total	18	100.0

Table 3.10: Children who were wasted according to CDC (2000) growth reference charts at initiation of ART according to clinic records

Z score	No of children *(N)*	Percentage (%)
Z score > -2SD* (mild wasting)	123	98.4
Z score < - 2SD (moderate wasting)	2	1.6
Total	125	100.0

* Standard Deviation

3.3.2. Underweight children at initiation of ARV

At initiation of ART, 52.8% (*N*=66) of the total number of children who took part in this study were mildly underweight according to CDC (2000) growth reference charts in comparison to 14.4% (*N*= 18) of children who were severely underweight (Table 3.11).

Table 3.11: Children who were underweight (weight/age) at initiation of ART based on CDC (2000) growth reference charts

Z score	No of children	Percentage

	(N)	*(%)*
Z score > -2SD* (mildly underweight)	66	52.8
Z score < -2SD (moderately underweight)	41	32.8
Z score < -3SD (severely underweight)	18	14.4
Total	125	100.0

* Standard Deviation

3.3.3. Stunting in children at initiation of ART

Of the total number of children who took part in this study, 75.2% (*N*=94), 14.4% (*N*=18) and 10.4% (*N*=13) were mildly, severely and moderately stunted respectively based on CDC (2000) growth reference charts (Table 3.12).

Table 3.12: Children who were stunted (height/age) according to CDC (2000) growth reference charts at initiation of ART

Z Score	No of children *(N)*	Percentage *(%)*
Z score >-2SD* (mild stunting)	94	75.2
Z score < -2SD (moderate stunting)	13	10.4
Z score < -3SD (severe stunting)	18	14.4
Total	125	100.0

* Standard Deviation

3.4 ANTHROPOMETRIC STATUS AND DISEASE PROGRESSION (BASED ON WHO/CDC STAGING) AT INITIATION OF ART.

3.4.1. Relationship between wasting and WHO disease staging at initiation of ART

Of the total number of children who took part in this study (*N*=125), 40% (*N*=50) had WHO staging documented in their medical files at initiation of ARVs. The majority of children 86% ((*N*=43), were symptomatic and 58% (*N*=29) were in WHO disease staging II and 28% (*N*=14) in stage III when they were initiated onto ARVs (Table 3.2).

It was also noted that of the total number of children (*N*=125), those children [40% (*N*=50)] who had WHO staging documented in their medical files at initiation of ARVs, 96% (*N*=48) of them were mildly wasted compared to the 4% (*N*=4) and 0% initiated with moderately and severely wasted nutritional status. Of the 96%, 58.3% (*N*=28) and 27.1% (*N*=13) were in WHO disease stages II and III respectively (Figure 3.1 and Table 3.13).

There were therefore more mildly wasted children initiated onto ART, the majority of whom were in WHO disease stages II and III. However, there was no significant difference in the relationship between wasting and WHO disease staging at initiation of ART (maximum likelihood chi-square = 0.889, p>0.05).

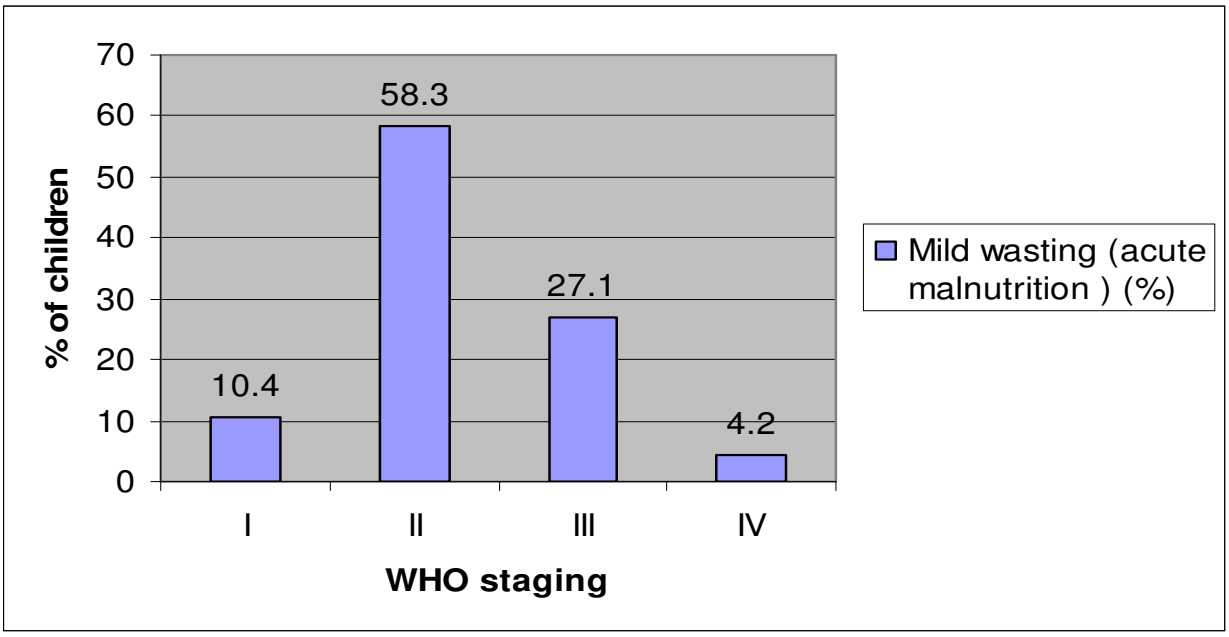

Figure 3.1: Comparison between mild wasting and WHO disease staging at initiation of ART

Table 3.13: Relationship between WHO disease staging and mild wasting at initiation of ART

WHO staging	Mild wasting	
	(N)	*%*
I	5	10.4
II	28	58.3
III	13	27.1
IV	2	4.2
Total	48	100

Chi-square = 0.889, p>0.05

3.4.2. Relationship between underweight and WHO disease staging at initiation of ART

There were more children 58% (*N*=29) who were symptomatic with normal activity (WHO disease staging II) than the 4% (*N*=2) who had reached the onset of AIDS (WHO disease staging IV) at initiation of ART (Table 3.14). There were more underweight children in WHO stage II compared to any other WHO disease stage (Table 3.14).

Table 3.14: Relationship between WHO disease staging and underweight at initiation of ARV therapy

WHO staging	Underweight							
	Mild		Moderate		Severe		Total	
	(N)	*(%)*	*(N)*	*(%)*	*(N)*	*(%)*	*(N)*	*(%)*
I	2	7.4	3	18.8	0	0	5	10
II	16	59.3	10	62.5	3	42.9	29	58
III	7	25.9	3	18.8	4	57.1	14	28
IV	2	7.4	0	0	0	0	2	4
Total	27	54	16	32	7	14	50	100

Chi-square = 7.625, p>0.05

Fifty-four percent (*N*=27) of the children across the different WHO disease stages were initiated onto ARVs while mildly underweight compared to 32% (*N*=16) and 14% (*N*=7) who were moderately and severely underweight respectively (Table 3.14 and Figures 3.3).

There was no significant difference in the relationship between underweight and WHO disease staging at initiation of ART (maximum likelihood chi-square = 7.625, p>0.05).

3.4.3 Relationship between stunting and WHO disease staging at initiation of ART

Seventy-eight percent (*N*=39) of the children across the different WHO disease stages were mildly stunted as compared to 10% (*N*=5) and 12% (*N*=6) who were moderately and severely stunted during ART initiation respectively. There were more stunted children in WHO stage II (*N*=29, 58%) (Table 3.15).

There was no significant difference in the relationship between stunting and WHO disease staging at initiation of ART (maximum likelihood chi-square = 6.615, p>0.05).

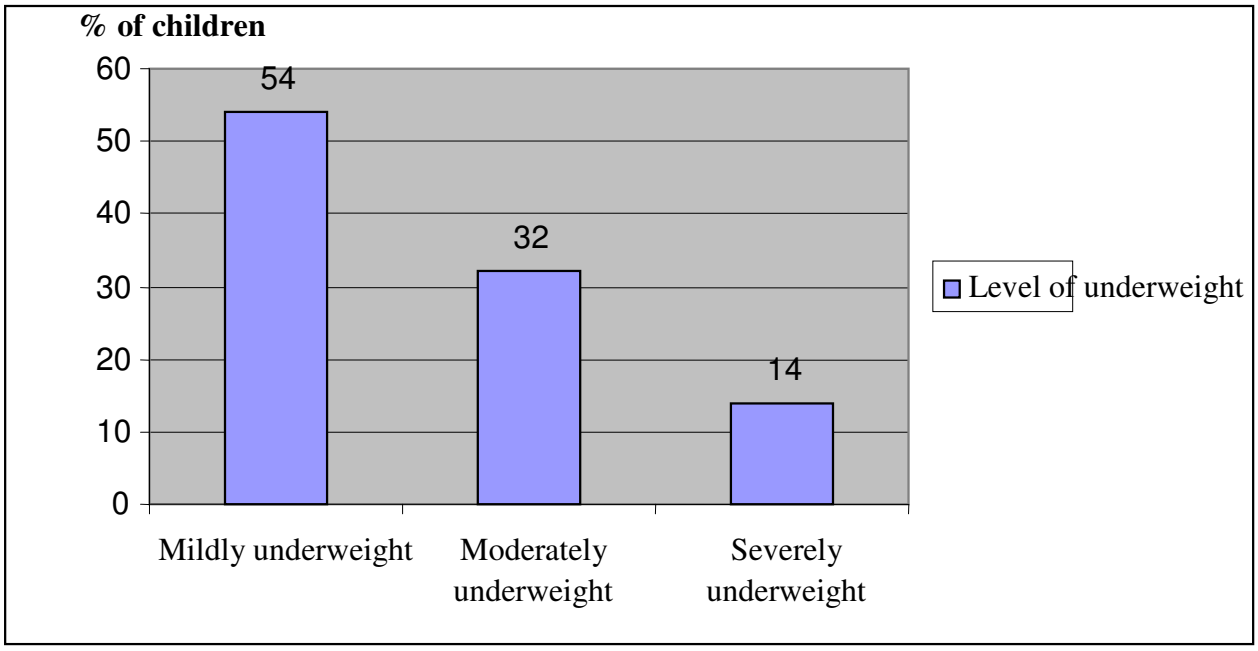

Figure 3.3: Children that were initiated onto ARV therapy under the various categories of underweight

Table 3.15: Relationship between stunting and WHO disease staging at initiation of ARV therapy

WHO staging	Stunting							
	Mild		Moderate		Severe		Total	
	(N)	(%)	*(N)*	(%)	*(N)*	(%)	*(N)*	(%)
I	4	10.3	0	0	1	16.7	5	10
II	21	53.8	5	100	3	50	29	58
III	12	30.8	0	0	2	33.3	14	28
IV	2	5.1	0	0	0	0	2	4
Total	**39**	**78**	**5**	**10**	**6**	**12**	**50**	**100**

Chi-square = 6.615, p>0.05

3.5. RELATIONSHIP BETWEEN CD4 PERCENTAGE AND UNDERWEIGHT AT INITIATION OF ART

Of the total number of children who took part in this study (*N*=125), 71.2% (*N*=89) were initiated onto ARVs using the CD4% guideline. Of these, 80.9%, (*N*=72) were children initiated onto ART with CD4 <15%, 54.2% (*N*=39) while mildly underweight, 27.8% (*N*=20) were moderately underweight and 18.1% (*N*=13) were severely underweight. A similar trend was observed in stunted children. There were more mildly stunted children initiated on ART in comparison to those who were moderately to severely stunted (Table 3.16) with CD4 < 15%.

There was however no significant difference in the relationship between CD4 percentage and stunting at initiation of ART (maximum likelihood chi-square = 2.988, p>0.05).

Table 3.16: Stunting and underweight using the CD4% guideline during initiation of ART

CD4%	Mildly underweight	Moderately underweight	Severely underweight
No of children with < 15% cells/mm³	39	20	13

%	54.2	27.8	18.1
	Mildly stunted	**Moderately stunted**	**Severely stunted**
No of children with < 15% cells/mm³	55	6	11
%	76.4	8.3	15.3

Chi-square = 2.988, p>0.05)

3.6. TRENDS IN WEIGHT AND CD4% CHANGES AFTER INITIATION OF ART

The findings of this study indicate that of the total number of children initiated on ART using CD4% <15% cells/mm³, in 80.9% (*N*=72) (Table 3.4), there was no correlation between weight changes and CD4 percentage changes (increase or decrease) on four consecutive CD4 count monitoring follow up visits at 3-5 month intervals. Weight trends tended to flatten out and remained consistent and had no significant impact on CD4% changes in children. The exponential increases and decreases in CD4% were not matched with increases in weight gain. Weight changes and CD4% were not dependent on each other. It was evident that for the children in this study, as CD4% fluctuated over time, weight remained more or less constant with negligible changes of approximately 1-2 kg of weight on average (Figure 3.4).

The findings also indicated that there was no relationship between CD4% and weight loss (average 1kg) on consecutive follow-up visits (Figure 3.5). This was observed only in children who had consistently lost weight during follow up (25.6%; *N*=32). This average weight loss of 1kg was accompanied by exponential increases and decreases in CD4% although there was no significant relationship between the two.

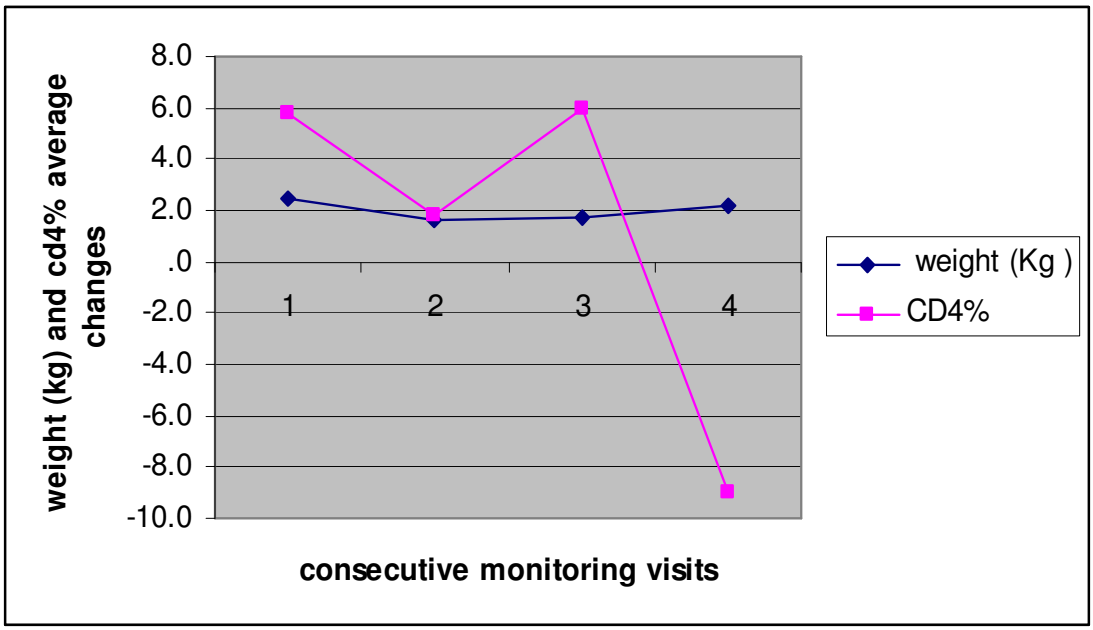

Figure 3.4: Trends in weight and CD4% changes following initiation onto ART.

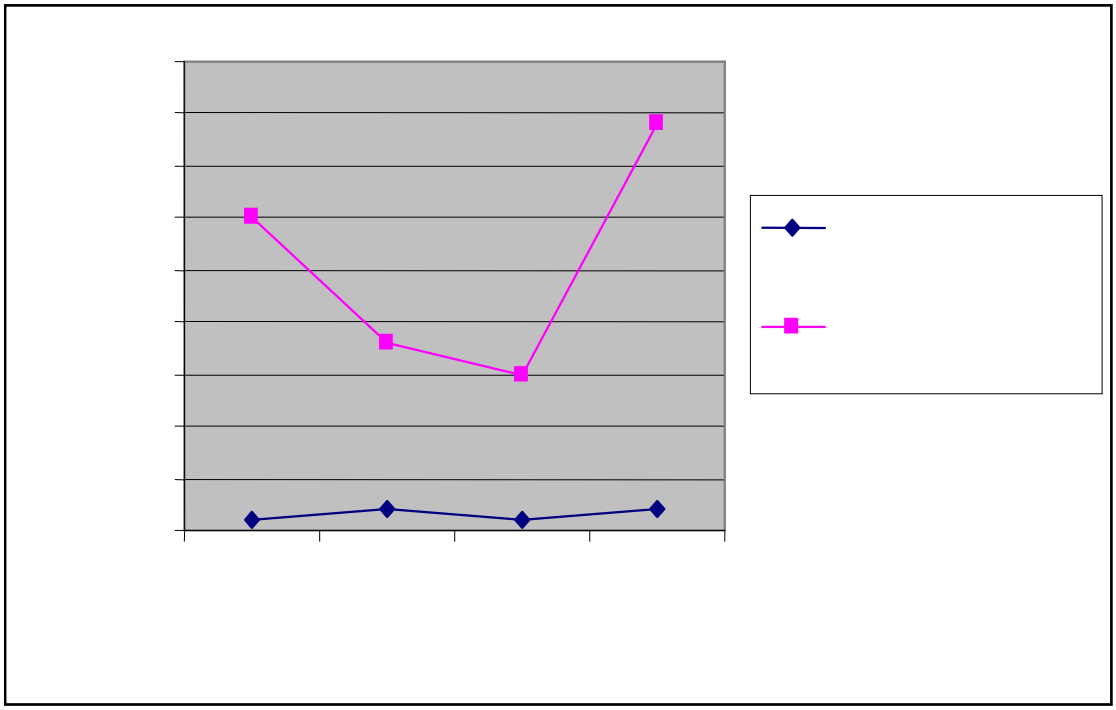

Figure 3.5: Trends in CD4% in children who lost weight

CHAPTER 4: DISCUSSION

4. DISCUSSION

The findings of the present study indicate that there was no significant relationship between WHO staging and anthropometric status at initiation of ART in children at the Mildmay Centre. It would therefore appear that anthropometric status, on its own, should not be used as a criterion for initiating ARV therapy. The complexity of the natural progress of the underlying disease and its impact on changes in anthropometric status may be more gradual, and anthropometric status may be less sensitive than other parameters, such as CD4 counts in detecting a change in disease severity and the need to initiate ARV treatment.

The majority of children were initiated onto ART when they were symptomatic (WHO disease stage II and III) and (CDC stages A and B). Very few children were initiated onto ART when they were not symptomatic (CDC stage N and WHO disease stage I respectively), and at the onset of AIDS/severely symptomatic (WHO disease stage IV and CDC stage C respectively). During the symptomatic stage, nutritional status is compromised and nutritional needs increase particularly as a result of inadequate food intake (e.g. due to loss of appetite), nutrient mal-absorption, altered metabolism and the effect of HIV on the body.[16, 25, 33] It is during this stage that nutritional status and CD4 count would be more likely to be affected in children living with HIV/AIDS.[43] Furthermore, a possible explanation for the least number of children being initiated on ART at the onset of AIDS or when they are severely symptomatic could be that most children would probably have died before treatment could be administered..

Children from all the different categories of malnutrition (i.e. mild, moderate or severe) were initiated onto ART. However, fewer children were initiated onto ART when their degree of malnutrition was moderate to severe compared to those initiated when mildly malnourished. The physiological difference between wasting and underweight could explain why more children were initiated onto ART when mildly wasted rather than moderately or severely wasted as was the case in stunting and underweight. In HIV/AIDS, wasting is a sign of disease progression and occurs following pronounced weight loss, and the reverse is true in that weight loss precedes wasting. Wasting is one of the leading manifestations of progressive disease[35] and is accompanied by loss of muscle mass as opposed to loss of fat when underweight. During wasting, the body burns muscle to provide the energy necessary to counteract infection, thus altering body metabolism and nutrient use. However, there are other factors e.g. clinical

assessments and opportunistic infections that would also be clinically considered during initiation of ART in children and not malnutrition alone.[4]

Based on CD4%, it was established that more children were initiated onto ART when mildly malnourished (i.e. mildly wasted, mildly stunted, mildly underweight). However, there was no correlation between weight change and CD4% during subsequent follow up visits i.e. weight remained constant - on average the weight change (loss and gain) was a negligible 1kg, with minimal CD4% changes, an indication that CD4% is independent of weight gain. Had there been a trend or correlation, the CD4% fluctuations would have been matched with weight fluctuations, therefore it is evident that there are other factors other than anthropometric status that affect CD4%. These findings support clinical trials which showed that nutritional status is independent of CD4 count contributing to high morbidity and mortality in malnourished children[46, 47]. However, some studies have shown that weight loss is associated with lowered CD4 count. Studies conducted in adults[30] found that weight loss occurred with CD4 >200 cells/mm³, supporting the findings in this study and the difference noted between trends seen in wasting and underweight children, suggesting that weight loss occurred even when CD4% was high, creating the variation between the mild, moderate and severe underweight. The fluctuating CD4% could be attributed to various factors including poor/inadequate dietary intake, frequent illness and disease progression.

The results showed that the vast majority of children were initiated on ART when mildly malnourished, and of these there were more mildly wasted children 96% (*N*=48) as opposed to mildly stunted 78% (*N*=39) and mildly underweight (54% (*N*=27). This finding may be an indication that wasting is more closely linked to CD4% in children during initiation of ART in comparison to stunting and underweight, an observation supporting the reason why wasting is one of the variables incorporated into WHO disease stages III and IV. This possible correlation requires more clinical investigation.

Most of the children who took part in this study were initiated on ART before the age of 2 years. This is in agreement with studies that have shown that by one year of age, 30% of untreated

children will die and by 2 years of age, 50% of children will die if untreated. At the Mildmay Centre, 80.0% of the children were already receiving treatment by the age of 2 years.
As stated earlier (section 2.4.2), the accurate sample size for this study should ideally have been *N*=186, however, a sample size of *N*=125 was used because anthropometric data, were not consistently recorded at initiation of ART and during follow up visits at the Mildmay centre. Height, in particular, was a missing variable in the medical records. This data gap in the centre's data management system presented a limitation to this study and is an indication that the monitoring of all anthropometric measurements needs to be improved. It was increasingly evident that height was not a priority measurement at the Mildmay centre in comparison to other parameters such as CD4% and weight. Often, children would go to the centre for treatment on a monthly basis, and unlike weight, height was taken at 3-6 months intervals; resulting in data gaps for height measurements. Without height measurements, anthropometric indices such as weight/height and height/age, vital for this study, could not be determined.

One possible reason for prioritizing weight and not paying much attention to height could be that some of the children's medication dosage is based on weight measurements at the Centre. However, it was occasionally documented in some of the children's medical records that anthropometry could not be conducted during some visits because the child was too weak to stand for long periods. Some of the children's medical files showed that height measurements tended to be inconsistent and varied tremendously between visits, rendering some of this data unreliable and therefore not suitable for use in this study. This resulted in a further reduction in the possible sample size. In a working environment such as that of the Mildmay Centre, staff turnover and rotation in the clinic are characterised by errors in judgment, regardless of the training provided in recording anthropometric measurements, especially height. Data accuracy is thus adversely affected, especially if data is collected retrospectively.

4.1 Study limitations

- One of the assumptions of this study was that the Mildmay centre had been consistently measuring and recording anthropometry (both height and weight) but it became increasingly evident that height was not a priority measurement, a critical assumption in

the data management system overlooked during protocol development. The sample size of 186 children was thus reduced to 125 mainly because on closer inspection of the files, 61 of the 186 files, had data missing. It is important to note that sampling had to remain random (and not stratified), therefore none of the remaining 164 patient files (those not originally selected) could be selected for inclusion in the sample because this would imply that the investigator could have created bias by looking for files with completed data and the sample selection exercise would no longer be random/applicable.

- This was a retrospective study and over the years due to staff changes, staff turnover and changes in departments at the centre, it was acknowledged that the weight and height measurements would have consequently been taken by different trained professionals with different levels of accuracy. This issue resulted in some files being excluded from the study.

CHAPTER 5: CONCLUSIONS AND RECOMMENDATIONS

5. CONCLUSIONS AND RECOMMENDATIONS

5.1 CONCLUSION

There was neither a significant difference between anthropometric status and ART initiation nor a relationship between CD4% and weight changes. This study indicates that anthropometric status alone cannot be used to determine when to initiate ART in children aged 2-12 years. However, in the absence of CD4 laboratory parameters to indicate when to initiate ART in children, the anthropometry index that can safely be relied upon is wasting in conjunction with WHO disease staging. Furthermore, the findings of the study indicated that, there were more mildly wasted children than any other group initiated onto ART. The safest course of action which can be recommended consequently, is to initiate moderately or severely malnourished children onto ART in resource limited areas. based on the finding that more children who were mildly wasted were initiated onto ART when anthropometric status was the only reliable indicator. In the absence of CD4 laboratory parameters, in resource-limited areas, moderate and severe wasting anthropometric status could be used concurrently with WHO disease staging II and III to initiate ART in children.

5.2 RECOMMENDATIONS

Nutrition assessments should form an essential component of routine care and treatment in people living with HIV/AIDS especially children at health care facilities. HIV/AIDS treatment and care service providers need to ensure that anthropometry including height is routinely, consistently, accurately captured and recorded in health facility data management systems.

Anthropometric status (moderate to severe wasting – weight for height) could be used concurrently with CDC and WHO disease staging, in resource limited areas (in absence of CD4 laboratory parameters) to initiate ART. However, anthropometric status on its own can not be used to initiate ART in children.

The link between nutrition and HIV/AIDS is well documented with nutrition continuing to play a vital role in the care, management and treatment of people with HIV/AIDS. Nutrition training and education at health care centres should therefore continue to be integrated and emphasized at

all stages of HIV/AIDS care, management and treatment. It is partly through improved nutrition knowledge that health care providers will gain greater understanding of this link and place more emphasis and priority on nutritional components e.g. comprehensive nutrition assessments, nutrition education and counselling in the context of HIV/AIDS in children.[3, 48]

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APPENDICES

APPENDIX 1: SAMPLE SIZE CALCULATION

Krejcie & Morgan (1970) produced a table for determining sample size (Table A1). Calculations are not required to use the table that is reproduced below. To establish the sample size required to be representative of 350 children, simply read the table at population size N = 360 (the upper limit of 350). The sample size *(N)* in this example is 186. This methodology is applicable to any population of a defined (finite) size.

Table A1: Required sample size, given a finite population, where N = population size and n = sample size

N - n	N - n	N - n	N - n	N - n
10 - 10	100 - 80	280 - 162	800 - 260	2800 - 338
15 - 14	110 - 86	290 - 165	850 - 265	3000 - 341
20 - 19	120 - 92	300 - 169	900 - 269	3500 - 346
25 - 24	130 - 97	320 - 175	950 - 274	4000 - 351
30 - 28	140 - 103	340 - 181	1000 - 278	4500 - 354
35 - 32	150 - 108	**360 - 186**	1100 - 285	5000 - 357
40 - 36	160 - 113	380 - 191	1200 - 291	6000 - 361
45 - 40	170 - 118	400 - 196	1300 - 297	7000 - 364
50 - 44	180 - 123	420 - 201	1400 - 302	8000 - 367
55 - 48	190 - 127	440 - 205	1500 - 306	9000 - 368
60 - 52	200 - 132	460 - 210	1600 - 310	10000 - 370
65 - 56	210 - 136	480 - 241	1700 - 313	15000 - 375
70 - 59	220 - 140	500 - 217	1800 - 317	20000 - 377
75 - 63	230 - 144	550 - 226	1900 - 320	30000 - 379
80 - 66	240 - 148	600 - 234	2000 - 322	40000 - 380
85 - 70	250 - 152	650 - 242	2200 - 327	50000 - 381
90 - 73	260 - 155	700 - 248	2400 - 331	75000 - 382
95 - 76	270 - 159	750 - 254	2600 - 335	100000 - 384

(Adapted from Krejcie & Morgan, 1970, pp.608)

As the population size *(N)* increases, the sample size*(N)* increases at a diminishing rate (plateau) and remains constant eventually at slightly more than 380 cases. There is little to be gained by extending the sample beyond approximately 380 cases or to warrant the extra expense and energy a larger sample would require.

APPENDIX 2: DATA CAPTURING TOOL

(a) Data entry (patient data)

The use of anthropometric indices as an alternative guide to initiating Anti Retroviral drugs (ART) in children at The Mildmay Centre, Kampala Uganda

Date of Data entry	
Interviewer ID	
Interviewee ID (File Number)	
Where participant lives? (Village, county/ district)	
Contact details (if any)	

<table>
<tr><td>Client No:</td><td colspan="2"></td><td></td></tr>
<tr><td>Age</td><td>Gender
M F</td><td>Date client first registered at Mildmay</td><td>Date child started ART</td></tr>
<tr><td>Duration on ART to date (months)
< 3
3-6
12
12-24
24-48
> 60</td><td>Weight (kg), day ART was started</td><td>Height (cm), day ART was started</td><td>WHO staging at the time ART was started
Stage I
Stage II
Stage III
Stage IV
Not indicated</td></tr>
<tr><td>CD4 count at the time ART was started</td><td colspan="3">CD4 % count at the time ART was started</td></tr>
</table>

RECORD OF HEIGHT AND WEIGHT ON EACH FOLLOW UP VISIT

Date	Weight (Kg)	Height (Cm)	Age	CD4 (%)	ARV Drug Regimen

RECORD OF WEIGHT AND HEIGHT BEFORE ART WAS STARTED

Date	Age	Weight	Height

ARV PROGRAMMES

PEPFAR	KTRSA	Min of Health	Self sponsored

RECORD IF CD4 % TAKEN BUT ART DELAYED

Date	CD4%	Age	Weight	Height	Reasons for delay if stated

NUTRITION SUPPORT

Number	Question	Answers		
5.1	Has the client ever enrolled on the food programmes?	YES	NO	
5.2	If yes, which programmes?	WFP	USAID (ACDI-VOCA)	Other: (name)
5.3	Has the child ever been referred to other centres for nutritional rehabilitation?	YES	NO	
5.4	If yes, were they admitted at the above centres?	YES	NO	
5.5	Has the child or child's caregiver ever received nutrition counseling and education?	YES	NO	
5.6	If yes, in which nutrition education topics?			