RELATIONSHIP BETWEEN DEPRESSION AND WHO CLINICAL STAGE OF HIV IN PATIENTS ATTENDING AMPATH CLINIC AT WEBUYE COUNTY HOSPITAL, KENYA

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DECLARATION

This thesis is my original work and has not been presented for a degree in any other university. No part of this thesis may be reproduced without the prior permission of the author and/or Moi University.

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ABSTRACT

Background: The Sub Saharan Africa prevalence of depression in HIV/AIDS is estimated at between 39 to 47 %, which is nearly two times higher than in HIV negative group. Depressive symptoms have been associated with risky behavior, non-adherence to medications, and shortened survival. Not much is known about the risk factors of depression in HIV/AIDS in Kenya. Thus the study was undertaken to find out the relation between depression and WHO clinical stage of HIV at Webuye county Hospital AMPATH clinic.

Broad objective: To establish the relationship between depression and WHO clinical stage of HIV among patients attending Webuye County Hospital comprehensive care clinic.

Setting: Webuye County Hospital AMPATH Clinic.

Method: This was a descriptive cross-sectional study in which 345 randomly selected HIV positive patients enrolled at AMPATH clinic Webuye were studied. A pre-structured questionnaire was used to collect social and demographic data, CD4 count and WHO clinical stage of HIV. Frequency and severity of depression was assessed using the patient health questionnaire (PHQ-9), which is a widely used validated tool for assessing and measuring depression. Chi-square test was employed in the analysis. Data analysis was done using software for data analysis and statistical computing known as R. $P<0.05$ was considered significant.

Results: Out of 345 analyzed, the median age was forty one years, males compromised 39.1% and 59.7% were married. The median CD4 count was 217. The prevalence of depression was 44.1%, among those with depression 88.2% had mild while 11.8% had moderate to severe depression. Higher initial CD4 count was found to lower the odds of depression, $p=0.031$. None of the other factors studied were associated with occurrence and severity of depression.

Conclusions: Depression is common among the HIV infected patients attending AMPATH clinic Webuye. Higher initial CD4 count was found to reduce the odds of depression. WHO clinical stage of HIV was not associated with depression.

Recommendations: All HIV positive patients should be screened for depression. People with lower CD4 at enrolment should be followed up closely and offered psycho-social and other support to prevent depression.

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DEDICATION

I dedicate this thesis to my wife Beatrice, sons Wakoli Jnr and Barasa, my mother Elicah and my late father William.

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ACRONYMS/ABBREVIATIONS

AIDS	Acquired Immunodeficiency Syndrome
AMPATH	Academic model providing access to healthcare
CD4	Cluster of Differentiation 4
CCC	Comprehensive Care Clinic
DSM-IV-TR	Revised fourth edition of the Diagnostic and Statistical Manual of Mental Disorders
HAART	Highly Active Antiretroviral Therapy
HIV	Human Immunodeficiency Virus
ICD	International Statistical Classification of Diseases and Related Health Problems
IREC	Institutional Research and Ethics Committee
MD	Major Depression
MDD	Major depressive disorder
PITC	provider initiated testing and counseling
PLWHA	People Living With HIV/AIDS
PHQ-9	Patient health questionnaire-9
WHO	World Health Organization

CHAPTER ONE: INTRODUCTION

1.1 Background

The HIV/AIDS pandemic has caused far-reaching effects in low-income countries. Sub-Saharan Africa has been particularly hard hit. In 2014, 69% of all people living with HIV resided in Sub-Saharan Africa, a region with only 12% of the global population (UNAIDS, 2015). Sub-Saharan Africa also accounted for 66% of new HIV infections and approximately two-thirds of AIDS-related deaths in 2014. In 2012, Kenya had an estimated 1.6 million people living with HIV, with a prevalence of 5.6%. AIDS related deaths in 2010 stood at sixty five thousand (NASCOP,2012).

The WHO immunological classification for established HIV infection is based on the CD4.The HIV associated immune-deficiency relates with CD4 as follows;

- Stage 1: CD4>500 non or not significant,
- Stage 2: CD4 of 350 to 499 mild,
- Stage 3: CD4 of 200 to 349
- Stage 4: Advanced, CD4<200 severe (WHO,2007).

The WHO clinical staging for established HIV infection is classified into four categories. Stage one: asymptomatic, in this stage the patient has no symptoms or only has generalized lymphadenopathy. Stage two: mild symptom such as recurrent upper respiratory tract and bacterial skin infections. Stage three: advanced symptoms, include features such as persistent oral candidiasis and current tuberculosis. Stage four: severe symptoms such as

extra-pulmonary tuberculosis and Kaposi sarcoma (WHO,2007). Further details are contained in the appendix.

It is estimated that 350 million people are affected by depression worldwide (WHO, 2012). At its most severe form it can lead to suicide and it's responsible for eight hundred and fifty thousand deaths every year (WHO, 2012). The World Health Organization (WHO) estimates depression to be the leading cause of disability as measured by Years Lost due to Disability (YLDs) contributing to almost 12% of all disability (WHO,2012) and it also predicts depression will be the leading cause of worldwide disability by the year 2020 (WHO,2011). It is also the second leading contributor to the global burden of disease as measured by Disability Adjusted Life Years: DALYS (the sum of years of potential life lost due to premature mortality and the years of productive life lost) in the age category of 15 - 44 years for both sexes combined (WHO,2012).The American Psychiatric Association's revised fourth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR) is the most widely used criterion for diagnosis of depression. According to DSM-IV-TR, there are two main depressive symptoms- depressed mood and anhedonia. At least one of these must be present to make a diagnosis of major depressive episode.

In Major depression (also known as unipolar or clinical depression) the patient may complain of either or both of two cardinal symptoms, diminished interest or pleasure in activities and depressed mood or sadness. If either or both of these are present then other complaints are sought, including the following: decreased ability to concentrate, appetite changes with weight changes (increase or decrease), fatigue or loss of energy, feelings of worthlessness or guilt, insomnia or hypersomnia, psychomotor agitation or retardation and recurrent thoughts of death or suicide.

The diagnosis of major depression is made if five of the above symptoms occur on most days for at least 2 weeks. Depressed mood or diminished interest or pleasure must be one of the five symptoms present.

There are many tools validated for diagnosing and assessing severity of depression. In Kenya the Patient Health Questionnaire-9 (PHQ-9), a brief dual-purpose instrument yielding DSM-IV diagnoses and severity has been validated for assessing DSM-IV depressive disorders and depression severity among adults living with HIV/AIDS in western Kenya (Monahan et al, 2009).

According to World Health Organization World Mental Health (WMH) Survey Initiative conducted in 18 countries to establish the global pattern on depression, 15% of the population from high income countries and 11% from low income countries were likely to get depression over their lifetime (Bromet et al., 2011). The prevalence of major depression episode was estimated at 28% and 20% in high income and low income countries respectively. The strongest demographic correlate in high-income countries was being separated from a partner and in low- to middle-income countries, was being divorced or widowed (Bromet et al, 2011).

1.2 Problem Statement

Depression is under recognized nearly up to fifty percent among patients attending medical outpatient clinics, especially in resource limited settings (Perez et al.,1990; Steven et al., 2003; Rodkjaer et al., 2010). It is the most prevalent psychiatric co-morbidity and a common cause of significant morbidity among people with HIV infection despite the advent of highly active antiretroviral therapy (AIDS education, 2012; Rabkin JG,2008,

Dube B et al., 2005). Patients with depression are at higher risk for co-morbid psychiatric, alcohol, and substance use-related disorders, particularly alcohol, cannabis, and cocaine use (Kelly B et al., 1998; Compton WM et al., 2000). Depression is also associated with decreased survival, impaired quality of life, decreased adherence to antiretroviral therapy (ART), longer hospital stays, more frequent medical visits to the hospital to attend to HIV related ailments, higher treatment cost and risk behavior (Rodkjaer et al 2008; Sherboune et al., 2000).

These factors coupled with the high prevalence of depression in HIV/AIDS estimated at between 39 to 47 % make depression to be a great challenge in our country (Gadanya & Sale 2013, Nakimuli-mpungu et al., 2011).

I had anecdotal evidence based on frequent management of HIV positive patients with depression at Webuye County Hospital, that there was high prevalence of depression in HIV positive patients seeking treatment at the Hospital. It is with this background that this study sought to give insight on the association of clinical stage of HIV and depression among patients enrolled at the study site AMPATH clinic Webuye County Hospital to help improve services.

1.3 Justification

In Kenya, there is limited data on the relationship between depression and WHO clinical stage of HIV. There is need to come up with locally based evidence on the levels of depression in HIV and the category of the patients most affected. This would guide the healthcare workers and management to come up with guidelines to screen for depression. Literature search yielded limited studies on depression in HIV especially on the clinical stage of HIV and depression in our set up.

The results of this study will give insight on the association of clinical stage of HIV and depression among patients enrolled at the study site AMPATH clinic Webuye County Hospital. This we hope to use to improve services at the AMPATH clinic in Webuye County hospital.

1.4 Research Question

What is the relationship between depression and immunological and WHO clinical stage of HIV among patients attending AMPATH clinic at Webuye County Hospital?

1.5 Objectives

1.5.1 Broad

To establish the relationship between depression and WHO clinical stage of HIV among patients attending Webuye County Hospital AMPATH clinic.

1.5.2 Specific Objectives

- To determine the prevalence and severity of depression in patients with HIV
- To determine the relationship between WHO clinical stage of HIV and CD4 level in patients with HIV with depression
- To compare the odds of depression in each of the WHO stages of HIV

CHAPTER TWO: LITERATURE REVIEW

It is estimated that between 15 and 40% of patients with HIV/AIDS have major depression, up to two fold higher than in the HIV un-infected persons (Angelino & Treismann, 2001).

HIV increases risk of developing depression through direct damage to sub-cortical brain areas, chronic stress, worsening social isolation, and intense demoralization (Cruess DG et al., 2005, Andrew AD & Glenn JT, 2012). HIV-related infections or malignancy (e.g. central nervous system (CNS) toxoplasmosis, lymphoma, cryptococcal meningitis or syphilis) may also cause depressive symptoms, and several of these conditions have been associated with the development of major depression (Andrew et al., 2001). Some reports suggest that incident depression across a given treatment period is more likely to affect adherence than baseline depression in predicting subsequent adherence levels (Kacanek et al., 2010).

Global

In the USA a meta-analysis of prevalence studies showed ranges of depression in HIV-infected individuals from 0% to 22.5% with an overall rate of depression of 9.4% in HIV-positive persons compared with a rate of 5.2% in the comparison group (Ownby et al., 2010). In Denmark, the rates of depression in HIV were in conformity with the global rates (Rodkjaer et al., 2010).

Many studies have been done worldwide and some have showed there is a relation between depression and HIV. However, the parameters assessed and the results are different. In USA, a study by Lyketsos CG et al (1996) found an increase in depressive symptoms as AIDS developed. There was a 45 percent increase in depressive symptoms over the baseline six months prior the onset of AIDS. The factors associated with depression in the USA studies were female sex, prior depression, a self-report of AIDS-related symptoms (such as rash and lymphadenopathy), concurrent unemployment, cigarette smoking, and limited social supports.

In Europe, symptomatic stage of HIV infection has been associated with an increased prevalence of depressive symptoms. The associated risk factors were stigmatization and recent infection (Maj, 1996).

Some studies have found no association between clinical and/or immunological stage of HIV and depression. In Jamaica 63 HIV positive participants were interviewed for depression using the Patient Health Questionnaire (PHQ-9), they found no association between depression and the factors explored: CD4 count, age, gender, antiretroviral treatment, living arrangement, marital status and major stressors explored (Clark et al., 2010).

Sub Saharan Africa

In Sub Saharan Africa, studies have found an association between depression with stage of HIV and CD4 count levels. Factors that have been associated with the prevalence and the severity of depression include: stage of the disease and CD4 count level, ability to afford medications, ability to tolerate HAART and other drugs in the management of HIV (Alemu ., et al 2012 ; Gadanya & Sale, 2008)

In sub Saharan Africa, in studies done in Nigeria, South Africa and Uganda on the prevalence of depression in HIV/AIDS, showed a prevalence of depression in HIV that varied between 39% and 47% (Gadanya & Sale, 2013, Nakimuli -mpungu et al., 2011, Nel & Kagee, 2013).

In a study done in South Africa on prevalence of depression in HIV: 40.4% of participants' demonstrated moderate to severe symptoms of depression as per cut-off scores recorded using the Beck Depression Inventory - Second Edition (BDI II) (Nel & Kagee, 2013).

In Cameroon, in a cross-sectional study involving 100 newly diagnosed HIV patients, in which depression was assessed using the nine-item Patient Health Questionnaire (PHQ-9). A CD4 of below 100 was associated with a 2.9 times increased odds of probable depression. Other factor associated with depression was history of alcohol abuse (L,akoa et al., 2013). In a large study carried out in Kenya, Namibia and Tanzania involving 3538 participants, 28% reported mild to severe depressive symptoms, with 12 % reporting severe depressive symptoms. Factors associated with depression in HIV were female gender, younger age, not being completely adherent to HIV medications, likely dependence on alcohol, disclosure to three or more people (versus one person), experiences of recent violence, less social support, and poorer physical functioning (Seth et al., 2013).

In eastern Uganda among 1017 HIV-infected participants assessed for depression using the Center for Epidemiologic Studies Depression Scale (CES-D), patients with severe immune suppression were found to have higher depression levels: patients with CD4 counts <50 cells/microl were more likely to be depressed. Other factors associated with depression were women >50yrs and those without an income (Kaharuza et al., 2006).

In a study done in semi-urban Uganda involving 618 participants, CD4 count level was not associated with depression. Factors associated with depression included: female gender, family history of mental illness, negative coping style, alcohol dependency disorder, food insecurity and stress (Kinyanda et al., 2011).

Kenya

A study in Kenya at Kenyatta National Hospital with a sample of 400, the prevalence of depression in HIV/AIDS among patients attending comprehensive care clinic using Beck

Depression Inventory - Second Edition (BDI II) was 47%, with prevalence of moderate and severe being 25.25% and 12.25% respectively (Nganga & Pauline, 2011).

In another Kenyan study done in western Kenya rates for PHQ-9 DSM-IV major depressive disorder (MDD), other depressive disorder(ODD) any depressive disorder were 13%, 21% and 34% respectively. In the above study PHQ-9 was validated for assessing DSM-IV depressive disorders and depression severity among adults living with HIV/AIDS in western Kenya (Monaham et al,2009).

In the literature search there was limited data on research done in Kenya assessing the relationship between depression and WHO clinical stage of HIV.

Depression is associated non adherence to ART, progress of immune-deficiency and poor weight gain, (Alemu et al., 2012). Patients with depression are at higher risk for co morbid psychiatric and substance use-related disorders, particularly alcohol, cannabis, and cocaine use. Furthermore, untreated depression in HIV/AIDS often leads to poor or noncompliance with any treatment given, including ARVs, which can lead to development of resistant strains of the HIV virus (Sherbourne et al., 2000 ; Rodkjaer et al., 2008). The risk of suicide mortality in HIV-infected persons is 3-5 times higher than in HIV-uninfected counterparts, despite the availability of ART (Rodkjaer et al., 2010).

CHAPTER THREE: DESIGN AND METHODOLOGY

3.1 Study Site

The study was undertaken at Webuye County Hospital's AMPATH clinic. The staff working in the clinic is composed of doctors, clinical officers, nurses, peer educators, lay counselors, pharmacist, health record officer and nutritionist. They serve an average of 100

patients aged 18 yrs and above per day. Most of patients are recruited through PITC and then referred to the AMPATH for long term care. The hospital is a tier 4 facility with a 217 bed capacity. It is located in Bungoma county and approximately 396 kilometers from the capital city of Kenya, Nairobi. It has a catchment population of 60894 persons.

3.2 Study Design

Descriptive Cross-Sectional Study

3.3 Study Population

All adult HIV/AIDS patients on follow up at Webuye County Hospital AMPATH clinic who met the inclusion criteria were eligible. The Webuye AMPATH clinic has 2502 patients above 18 yrs on HAART.

3.4 Inclusion Criteria

- The participants were HIV-positive, at least 18yrs and willing to give consent.

3.5 Exclusion Criteria

- Clinically (physically) unstable patients in need of urgent medical attention.

3.6 Sample Size:

Sample size was calculated using the fisher's method of sample size calculation (Fisher, 1925).

$$n = \frac{z^2 \times p\,(1-p)}{\quad}$$

$$d^2$$

n= required sample size

z = confidence level at 95% (standard value of 1.96)

p = estimated depression rate 34% (based on a study done in western Kenya) (Monaham et al.,2009).

d = margin of error at 5%

$n= (1.96^2 * 0.34*0.66))/0.05^2$

n=345

Since the sampling frame is not static we don't adjust the sample size.

3.7 Sampling Procedure:

In this study, a systematic random sampling technique was employed in the recruitment of the study subjects. Data was collected two times a week which were the days when adults were mostly seen, for 24 weeks which was the time available for data collection, multiplying the two gives 48 days in which to collect data. To get the number of participants to be seen per day we divided the sample size 345 by 48, this gives 7.186 persons per day, rounded up to 8 participants per day. Dividing 8 with the number of patients seen in a day gives 12.5**,** rounded up to 13; this means every 13th participant was recruited. The first participant was the number chosen from a box with numbers numbered 1 to 13.

3.8 Data Management and Statistics

3.8.1 Data collection procedure;

Webuye is a cosmopolitan town where most of the inhabitants communicate in Swahili and English, hence data was collected in the two languages.

The data was collected from September 2014 to march 2015, by the principal investigator assisted by clinical officers who were trained on how to get an informed consent and how to administer the questionnaire.

Upon arrival at the clinic, eligible participants were informed about the study and their consent sought. Those who declined were reassured and offered normal clinic service. For consenting participants normal clinic services were offered before data collection. The information that was collected directly from the patient through the questionnaire include: age, gender, marital status, occupation, alcohol abuse using the CAGE questionnaire and level of education. WHO clinical stage and the CD4 count at the initiation of care and the current ones were got from the participants files, then entered into the data collection tool.

PHQ-9 a validated and widely used tool for screening for depression was used to assess the frequency and severity of depression.

PHQ-9 Depression Severity: This is calculated by assigning scores of 0, 1, 2, and 3, to the response categories of not at all, several days, more than half the days, and nearly every day respectively. PHQ-9 total score for the nine items ranges from 0 to 27. Has the following cut off points for assessing depression severity; (0-4) none or minimal, (5-9) mild, (10-14) moderate, (15-19) moderately severe and (20-27) severe.

Alcohol abuse was screened using the CAGE (Cutting down, Annoyance by criticism, Guilty feelings, Eye-openers) questionnaire. This instrument includes four questions:

(i) Have you ever felt you should cut down your drinking?

(ii) Have people annoyed you by criticizing your drinking?

(iii) Have you felt bad or guilty about your drinking?

(IV) Have you ever had a drink first thing in the morning to steady your nerves or get rid of a hangover (eye-opener)?

Alcohol abuse is diagnosed if there are at least two positive responses. The CAGE has been shown to have a sensitivity of 84.4% and a specificity of 93.1% to detect alcohol-related problems at this threshold of 2 positive responses (Amaral et al., 2004).

3.8.2 Data management and analysis

The data were collected using interviewer administered questionnaires, then entered in the primary investigator personal computer in coded excel data base, cleaned and stored. Data analysis was done using software for data analysis and statistical computing known as R (R Core Team, 2015). Descriptive statistics (frequencies, means and standard deviation) was used to summarize the data. Chi-square test was used to assess the relationship between depression and categorical variables. Continuous variables were assessed for normality using Shapiro-Wilk test. Association between continuous and categorical variables was assessed using two sample t test and two sample Wilcoxon rank sum test.

Some continuous variables such CD4 and PHQ9 score were categorized using clinically acceptable limits. CD4 was categorized as <200 and ≥200 cells per cubic mm, and PHQ9 depression scores were categorized as <10 and ≥10.

Results were considered significant at $p<0.05$. Findings are presented in the form of tables, bar graphs and pie-charts.

3.9 Ethical considerations;

Approval: The study was approved by the Moi University's institutional research and ethics committee (IREC) and permission to conduct the study at the site was sought from AMPATH.

Risks: Considering that this is a descriptive study, no intervention was undertaken thus the study participants who may have had concerns about possible harm were assured.

Benefits: All the findings and their significance were discussed with the patient. Those patients who screened positive for moderate depression and above were referred to the psychiatric clinic for confirmation and management.

Consent: Enrollment into the study was on a voluntary basis after seeking an informed consent. No persuasion or monetary offers were made. Those that opted not to participate in the study had their decision respected, were offered their routine clinic services.

Confidentiality: Serial numbers and not names were used on the questionnaire and data collection form. The data collected was treated with confidentiality.

CHAPTER FOUR: RESULTS

A total of 345 participants were included in the analysis. The median age of the participants was 41.0 (IQR: 35.0, 48.0) years with a minimum and a maximum of 18.0 and 81.0 years respectively. Male participants represented 39.1% giving a1:1.6 ratio of male to female in the study.

Female participants median age was 39.0 (IQR: 34.3, 47.0) years while male participants median age was 42.0 (IQR: 36.0, 48.5) years.

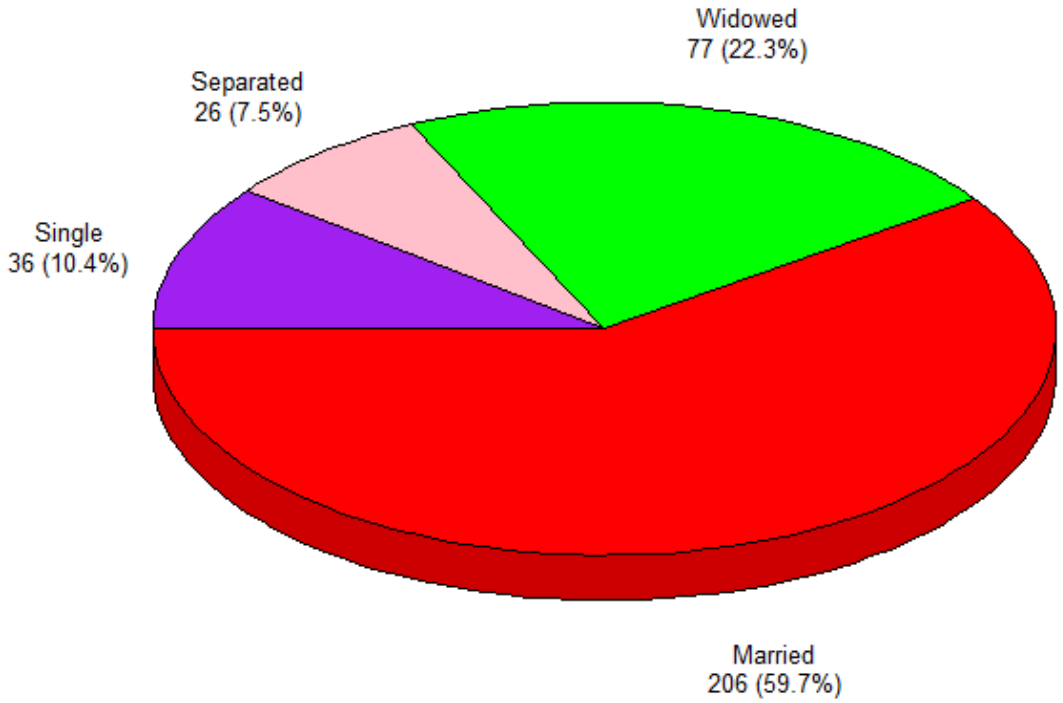

Figure 1: Distribution of participants by marital status

Majority of the participants, 206 (59.7%), were married. Slightly more than one fifth of the participants, 22.3%, were widowed, and 7.5% were separated. Single participants constituted 10.4% (Figure 1).The other socio-demographic characteristics studied; BMI, level of education and employment status, were not associated with depression.

Participants were diagnosed a median duration of 6.0 (IQR: 4.0, 8.0) years ago.

HIV disclosure status was assessed, 95.9% had disclosed their HIV status to at least someone. Those who disclosed had done so to a median number of 3.0 (IQR: 2.0, 6.0) persons with a minimum of 1.0 and a maximum of over 10.0 persons disclosed to.

The WHO clinical stages at enrollment as well as the current clinical stages were assessed. The results were as presented in Figure 2.

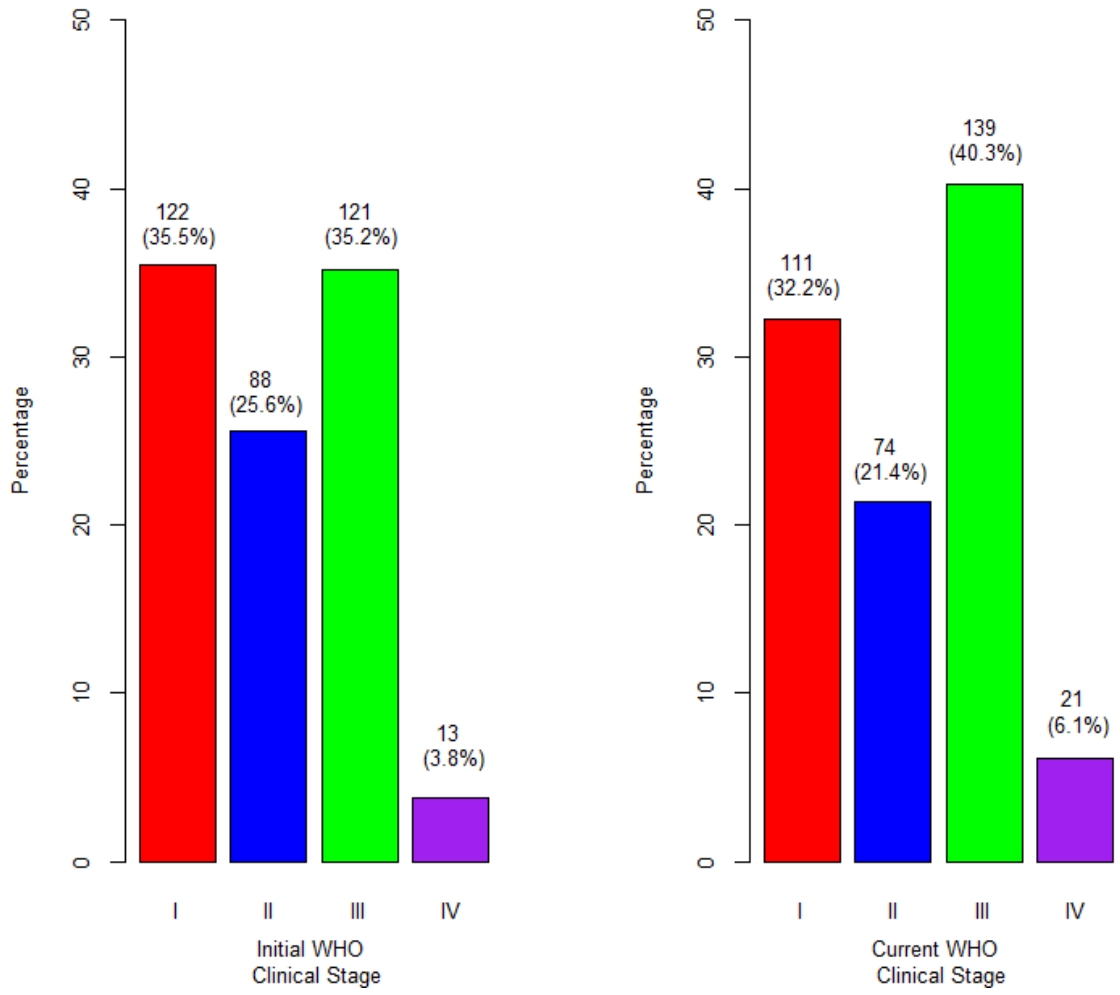

Figure 2: WHO clinical stage

More than one third of the participants were in WHO clinical stage I at enrollment. A similar proportion was seen for WHO clinical stage III. One quarter of the participants were in WHO clinical stage II. Less than 10% were in WHO clinical stage IV.

Table 1: Transition from initial WHO clinical stage to the current WHO clinical stage

	Current WHO stage				
Initial WHO Clinical stage	**I**	**II**	**III**	**IV**	**Total**
I	111 (91.0%)	4 (3.3%)	7 (5.7%)	0	122 (35.5%)
II		69 (78.4%)	17 (19.3%)	2 (2.3%)	88 (25.6%)
III			115 (95.0%	6 (5.0%)	121 (35.2%)
IV				13 (100%)	13 (3.8%)
Total	111 (32.25)	73 (21.4%)	139 (40.3%)	21 (6.1%)	344 (100%)

Four and seven of the participants moved from WHO clinical I to stages II and III respectively. Similarly seventeen and two of the participants moved from stage II to stages III and IV respectively. Six of the participants moved from stage III to stage IV (Table 1).

Table 2: CD4 co morbidities and alcohol abuse

Variable		Sample size	n (%) or Median (IQR)
Initial CD4	<200	327	147 (45.0%)
	≥200		180 (55.0%)
Presence of co morbidities		345	26 (7.5%)
Alcohol abuse		345	25 (7.2%)

The median initial CD4 count was 217.0 (IQR: 96.5, 414.5) cells per cubic mm.

Less than 10% of the participants had co morbidities present and 7.2% had history of alcohol abuse.

The median PHQ9 score measure of depression was 4.0 (2.0, 6.0).

The prevalence of depression was 44.1% (95% CL: 38.7%, 49.5%). Among those with depression 88.2% had mild while 11.8% had moderate to severe depression.

Table 3: Factors associated with depression

		Depressed		
Variable		**Yes (152, 44.1%)**	**No (193, 55.9%)**	**P**
Age		40.7 ± 8.8	41.9 ± 10.5	0.258
Gender	Male	57 (42.2%)	78 (57.8%)	
	Female	95 (45.2%)	115 (54.8%)	0.660
Married	Yes	96 (46.6%)	110 (53.4%)	
	No	56 (40.3%)	83 (59.7%)	0.295
Initial CD4		204.0 (84.2, 349.8)	223.0 (119.0, 477.0)	0.031
Initial CD4	≥200	76 (42.2%)	104 (57.8%)	
	<200	70 (47.6%)	77 (52.4%)	0.387
Years since HIV diagnosis		6.0 (4.0, 8.0)	6.0 (3.0, 8.0)	0.743
Disclosed	Yes	148 (44.7%)	183 (55.3%)	
	No	4(28.6%)	10 (71.4%)	0.359
Initial WHO stage	I	47 (38.5%)	75 (61.5%)	
	II	42 (47.7%)	46 (52.3%)	0.480
	III	57 (47.1%)	64 (52.9%)	
	IV	6 (46.2%)	7 (53.8%)	
Current WHO stage	I	43 (38.7%)	68 (61.3%)	
	II	34 (45.9%)	40 (54.1%)	
	III	64 (46.0%)	75 (54.0%)	0.533
	IV	11 (52.4%)	10 (47.6%)	
Presence of co morbidities	Yes	11 (42.3%)	15 (57.7%)	
	No	141 (44.2%)	178 (55.8%)	1.000
Alcohol abuse	Yes	12 (48.0%)	13 (52.0%)	
	No	140(43.8%)	180 (56.2%)	0.839

The only factor that was associated with depression was the initial CD4 where participants diagnosed with depression had a significantly lower initial median CD4 compared to those

who were not diagnosed with depression, 204.0 (IQR: 84.2, 349.8) cells per cubic mm vs. 223.0 (IQR: 119.0, 477.0) cells per cubic mm, p=0.031.

Table 4: Factors associated with severity of depression

		Severity of Depression		
Variable		**Mild (134, 88.2%)**	**Moderate/Severe (18, 11.8%)**	**P**
Age		40.4 ± 8.5	43.1 ± 11.0	*0.328*
Gender	Male	51 (89.5%)	6 (10.5%)	0.897
	Female	83 (87.4%)	12 (12.6%)	
Married	Yes	86 (89.6%)	10 (10.4%)	0.651
	No	48 (85.7%)	8 (14.3%)	
Initial CD4		*155.5(82.0, 301.8)*	*327.5 (209.2, 388.0)*	*0.016*
Initial CD4	≥200	62 (81.6%)	14 (18.4%)	0.016
	<200	68 (97.1%)	2 (2.9%)	
Years since HIV diagnosis		6.0 (4.0, 8.0)	6.0 (3.2, 8.8)	0.995
Disclosed	Yes	131(88.5%)	17 (11.5%)	0.399[f]
	No	3 (75.0%)	17 (25.0%)	
Initial WHO stage	I	40 (85.1%)	7 (14.9%)	0.576[f]
	II	39 (92.9%)	3 (7.1%)	
	III	49 (86.0%)	8 (14.0%)	
	IV	6 (100%)	0 (0.0%)	
Current WHO stage	I	36 (83.7%)	7 (16.3%)	0.592[f]
	II	32 (94.1%)	2 (5.9%)	
	III	56 (87.5%)	8 (12.5%)	
	IV	10 (90.9%)	1 (9.1%)	
Presence of co morbidities	Yes	11 (100%)	0 (0.0%)	0.363[f]
	No	123 (87.2%)	18 (12.8%)	
Alcohol abuse	Yes	10 (83.3%)	2 (16.7%)	0.636[f]
	No	124 (88.6%)	16 (11.4%)	

f – Fisher's exact P-value was reported because the expected value of at least one cell of the created 2x2 table was <5, a violation of Chi Square assumptions.

Among respondents with depression higher initial CD4 was significantly associated with moderate to severe depression, 327.5 (IQR: 209.2, 388.0) vs. 155.5 (82.0, 301.8) cells per cubic mm, p=0.016.

Those who had initial CD4≥200 were more likely to have moderate to severe depression, 18.4% compared to 2.9% among those who had <200 cells per cubic mm p=0.016.

Given that the initial CD4 was the only covariate that was associated with depression we did not fit an adjusted regression model. We however fitted a model to assess the direction and quantify the effect of CD4 on depression.

The effect of CD4 on the presence of depression was protective, odds ratio equal to 0.91 (95% CL: 0.83, 0.98) per 100 cells of CD4 count between subjects. This means that, comparing two participants who have a 100 cells difference between each other showed that the one with higher CD4 was up to 9% less likely to be diagnosed with depression.

On further analysis higher initial CD4 was not associated with severity of depression, odds ratio 1.16 (95% CL: 0.95, 1.40). The other factors showed no association with severity of depression.

CHAPTER FIVE: DISCUSSION

Prevalence of Depression

The prevalence of depressive disorders among patients attending AMPATH clinic at Webuye County Hospital was 44.1%. The study replicates previous findings concerning the prevalence of depressive disorders among People Living with HIV/ AIDS (PLWHs) in Sub-Saharan Africa in particular.

The prevalence of depression was 56.7% in Nigeria in a study on the prevalence and correlates of depressive disorders among people living with HIV/AIDS (Shittu et al, 2013).In a study done in Ethiopia on the prevalence and associated factors among HIV/AIDS patients attending ART clinic, the prevalence was 38.94% (Eshetu et al., 2015). In Malaysia, Tung Yee while studying depression among HIV patients in University of Malaysia Medical Centre found a prevalence of 32% (Tung et al., 2009). In Kenya the prevalence of depression was 34% in a study done to validate PHQ-9 in a population with HIV/AIDS (Monaham et al., 2009). The above studies used PHQ-9 to assess for depression. Lower values have been reported in Uganda and Zambia at 8.1% and 9.6% respectively (Chikezie et al., 2013). The two studies however, used International Diagnostic Criteria to make a diagnosis of depression.

In other studies done in Nigeria, South Africa and Uganda the prevalence of depression in HIV/AIDS varied between 39% and 47%. (Gadanya et al, 2008 ; Nel & Kagee 2013 ; Nakimuli-Mpungu et al,2011) . As expected prevalence rates based on DSM-IV diagnostic criteria may be lower than those based on screening instruments. The variation in

prevalence rate may be due to differences in methodology and subject characteristics (Arseniou et al,2014 ; Judd & Mijch, 1994).

The high prevalence of depression implies a need for regular screening for depression.

Severity of Depression in HIV/AIDS

Majority of the respondents with depression had mild levels at 88.2% while 11.2% had moderate to severe depression. The findings mirror recent studies. In Nigeria in a study on the prevalence and correlates of depressive disorders among people living with HIV/AIDS the severity of depression was similar, where 13% of the respondents were severely depressed (Shittu et al, 2013). In a study done in South Africa on prevalence of depression in HIV; 40.4% of participants' demonstrated moderate to severe symptoms of depression as per cut-off scores recorded using the Beck Depression Inventory - Second Edition (BDI II) (Nel & Kagee, 2013).

CD4 count and Depression

Studies on the association between CD4 count and depressive disorder have largely focused on the impact of depressive disorder on CD4 count as a factor in disease progression (Ironson et al, 2005; Ickovics et al, 2001) and not on the impact of CD4 count on depressive disorder. The few studies that assessed the association of CD4 count on depression used the current CD4 count as opposed to the initial CD4 count used in this study. The studies had conflicting results; some showed an association while others showed no association (Maj M , 1996), (Tung et al., 2009, Lckovics et al., 2001). A review of literature in this study did not find studies that used the initial CD4 count.

Clinical Stage of HIV/AIDS

In this study, there was no association between the clinical stage of HIV and depression occurrence or severity. Other studies that have assessed the effects of clinical stage of HIV/AIDS on depression have yielded inconsistent results. The absence of an association may be related on the one hand to the heightened likelihood of adjustment problems (learning of HIV status, disclosure of HIV status, introduction to medication) , manifesting as depression in the early stages of the infection, and on the other to the heightened presence of depressive-like symptoms in the more severe stages of the disease. In other words, there are different risk factors along the spectrum of HIV disease progression that would contribute to a heightened risk for depressive symptoms. In a study done in Malaysia and Jamaica using PHQ-9 clinical stage of HIV was not associated with depression (Tung et al., 2001 Clarke et al., 2010). In USA in a meta-analysis of ten studies examining the relationship between HIV infection and risk for depression, there was no association between depression and stage of HIV disease (Ciesla et al., 2001).

Several other studies have shown an association. In Europe Symptomatic stage of HIV infection has been associated with an increased prevalence of depressive symptoms (Maj M, 1996) .In a two-year prospective study of major depressive disorder in HIV-infected me, Major Depression rates were low in patients whose disease had not evolved to AIDS (Atkinson et al., 2008). In a study involving 60 HIV positive women with AIDS symptoms and 60 HIV positive without AIDS symptoms the prevalence of MD was higher in the symptomatic group (38.3%) than in the asymptomatic group (13. 3%) (Arseniou et al.,

2011). In some African studies symptomatic stages of HIV were linked with depression in HIV (Gaddanya et al., 2008).

The lack of association between WHO clinical stage of HIV and depression in this study could be explained by the combination of the following findings in this study; comparatively lower age of the participants (median age 41 years), high disclosure status (95.9%), low numbers of participants in WHO clinical stage IV, low transition rates of participants to higher WHO clinical stages and use of HAART.

Socio-demographic and other clinical factors

In this study, there was lack of association between the other clinical and socio-demographic factors and depression occurrence and severity. Other studies that have assessed the effects socio-demographic factors and depression have yielded inconsistent results.

Some studies have found higher rates of depression in HIV in the following category of patients; patients older than 50 years, in widows, females and patients' likely dependant on alcohol (Kinyanda et al 2011; WHO, 2007 ; Arseniou et al., 2014 ; Hinkin et al 2001) .While other studies have found no association between the socio-demographic and clinical parameters studied (Chikezie et al., 2013). The lack of association in this study could be explained by the comparatively lower age of the participants, lower rates of alcohol abuse, lower numbers of widows and the different population characteristics compared to the studies that reported associations.

CHAPTER SIX: CONCLUSIONS AND RECOMMENDATIONS

6.1 CONCLUSIONS

Depression is common among the HIV infected patients attending AMPATH clinic at Webuye and higher initial CD4 count was found to reduce the odds of depression. WHO clinical stage of HIV was not associated with depression

6.2 RECOMMENDATIONS

1. All patients should be screened for depression In HIV care setting.
2. Patients should be enrolled in care as early as possible, with higher CD4s, as higher CD4 reduces the odds of depression.
3. Patients with lower CD_4 count at enrolment should be offered psycho-social and other support to prevent depression.

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APPENDICES

1. CONSENT

INTRODUCTION AND CONSENT

Hello. I am Dr Simon Kisaka and I am a student at Moi university school of medicine. I am conducting a survey on the relationship between depression and the different stages of HIV/AIDS. We hope to use this information to assist clinicians screen and manage depression in HIV, this we hope will lead to better outcomes for the patients. I am doing this research at Webuye county hospitals' AMPATH clinic and will compare with other surveys done earlier. I request your permission to be involved in the study. The study involves you filling a questionnaire that will be used to assess if you are depressed.

Whatever information that you will provide will be kept confidential and will only be shared with members of our study team. Your identity will be kept secret. Your participation in this study is entirely voluntary and you can stop me anytime for any clarification you might need or if uncomfortable to continue. However, I hope that you will participate in this study to the end.

At this time, do you want to ask me anything about this study?

Consent:

I, the undersigned having being informed about this study to my satisfaction and all my questions and concerns having been addressed, do give to participate in this study.

Signed: Date:

Signature of interviewer: Date

2. **Consent-Swahili translation**

Utangulizi na ridhaa

Hello. Mimi ni Daktari Simon Kisaka na pia mwanafunzi wa chuo kikuu cha Moi shule ya matibabu. Mimi nafanya utafiti kuhusu uhusiano kati ya unyogovu na vitengo mbalimbali za UKIMWI. Tunatarajia kutumia habari hii kusaidia wauguzi kuchunguza na kusimamia unyogovu katika wagonjwa wa UKIMWI, hii tunatumani itasababisha matokeo bora kwa wagonjwa. Mimi nitafanya utafiti huu katika hospitali ya wilaya ya Webuye na kulinganisha na tafiti nyingine zilizofanyika awali . Naomba ruhusa yako ya kushiriki katika utafiti. Utafiti ni pamoja na wewe kujaza dodoso ambazo zitatumika kutathmini kama wewe una huzuni.

Taarifa zote zenye utatoa zitakuwa siri na zitabaki na wanachama wa utafiti timu yetu. Utambulisho wako itakuwa siri. Ushiriki wako katika utafiti huu ni hiari kabisa na unaweza kuacha kuendelea kwa utafiti wakati wowote bila ufafanuzi wowote. Hata hivyo, mimi matumaini kwamba wewe kushiriki katika utafiti huu hadi mwisho.

Kwa wakati huu, unataka kuuliza mimi chochote kuhusu utafiti huu?

ridhaa:

Mimi niliyetia sahiihapo chini nimeelezwa juu ya utafiti na nimeridhika na majibu niliyopewa.Natoa idhini ya kushiriki katika utafiti huu.

Saini : Tarehe:

Sahihi ya mhojaji : Tarehe

3. Study questionnaire

Socio-Demographic data.

Date.....

Age..... Gender/Sex Male ☐ Female ☐

Weight .....Height..... BMI.....

Marital Status; Single……. Married/cohabiting…….widowed……

Separated/divorced…… No of children……

Level of education; No education……..

Primary……..

Secondary…..

Tertiary……

Employment status; formally employed.....

Cash crop farmer.....

Casual labourer.....

Self employed.....

Unemployed.....

Disclosure; Yes…….. No….. Number Disclosed…….

Clinical data

Date enrolled on HIV care.....

Duration of HIV infection (yrs).....

Nadir CD4 count……. Current CD4.....

WHO stage (initial)..... Current WHO stage.....

HAART Regimen (i)..... Duration.....

(ii)..... Duration.....

(iii)..... Duration.....

Co morbid conditions;

4. Alcohol abuse (CAGE) questionnaire

(i) Have you ever felt you should cut down your drinking?

(ii) Have people annoyed you by criticizing your drinking?

(iii) Have you felt bad or guilty about your drinking?

(iv) Have you ever had a drink first thing in the morning to steady your nerves or get rid of a hangover (eye-opener)?

Total:

Other substance use; Y/N. If yes which one.

5. PATIENT HEALTH QUESTIONNAIRE (PHQ-9)

S/NO;_____ **DATE_____**

Over the last 2 weeks, how often have you been Bothered by any of the following problems? (use "× " to indicate your answer)	Not at all	Several days	More than half the days	Nearly every day
1.Little interest or pleasure in doing things	0	1	2	3
2.Feeling down, depressed, or hopeless	0	1	2	3
3.Trouble falling or staying asleep, or sleeping too much	0	1	2	3
4.Feeling tired or having little energy	0	1	2	3
5.Poor appetite or overeating	0	1	2	3
6.Feeling bad about yourself or that you are a failure or have let yourself or your family down	0	1	2	3
7.Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
8. Moving or speaking so slowly that other people could have noticed. Or the opposite being so fidgety or restless that you have been moving around a lot more than usual	0	1	2	3
9.Thoughts that you would be better off dead, or of hurting yourself	0	1	2	3

FOR OFFICE CODING 0 + _____ + _____ + _____ =Total Score: _____

10. If you checked off Not difficult at all_____

Any problems, how difficult have these somewhat difficult_____

Problems made it for you to do Very difficult_____

Your work, take care of things at home, Extremely

difficult_____

Or get along with other people

6. SWAHILI VERSION- (PHQ-9)

Katika kipindi cha wiki mbili zilizopita ni mara ngapi umesumbuliwa na matatizo haya yafuatayo? (Tumia " ✔ " ilikuashiria jibulako)	Haija tokeza kabisa	Siku kadhaa	Zaidi yanusu yasikuhizo	Takriban kila siku
1. Kutokuwa na hamu au raha yakufanya kitu	0	1	2	3
2. Kujisikia tabu sana au kukata tama	0	1	2	3
3.Matatizo ya kupata usingizi au kuweza kulala au kulala sana	0	1	2	3
4. Kujisikia kuchoka au kutokuwa na nguvu	0	1	2	3
5. Kutokuwanahamuyakula au kulasana	0	1	2	3
6. Kujisikia vibaya-au kujiona kuwa umeshindwa kabisa au umejiangusha au kuikatisha tama familia yako	0	1	2	3
7. Matatizo ya kuwa makini kwa mfano unaposoma gazeti au	0	1	2	3

kuangalia TV				
8.Kutembea au kuongea taratibu sana mpaka watu wakawa wameona tofauti? Au kinyume chake kwamba hutuliza nina unahangaika sana kulikoili vyo kawaida	0	1	2	3
9.Mawazo kuwa niafa dhali zaidi ufe au ujidhuru kwa namna Fulani	0	1	2	3

KIDODOSI JUU YA AFYA YA MGONJWA -9 (PHQ-9)

FOR OFFICE CODING 0 + _____ + _____ + _____ =Total Score: _____

Kama ulitia alama matati zo yoyote, matatizo hayo yamefanya iwevigumu kivipi kwako kufanya kazi yako, kushughulikia vitu nyumbani, au kutangamanana watu wengine?

Sio ngumu hataki dogo … Ngumu kiasi … Ngumu sana … Ngumu zaidi

Imetengenezwa na Drs. Robert L. Spitzer, Janet B.W. Williams, Kurt Kroenkenawenza wake, naruzukuyakielimukutokakwa Pfizer Inc. Hakuna kibali kinachohitaji kaili kuzalisha upya, kutafsiri au kuonyesha au kusambaza

7. **WHO clinical staging of HIV/AIDS for adults and adolescents with confirmed HIV infection**

Clinical stage 1

Asymptomatic

Persistent generalized lymphadenopathy

Clinical stage 2

Moderate unexplained weight loss (<10% of presumed or measured body weight)

Recurrent respiratory tract infections (sinusitis, tonsillitis, otitis media and pharyngitis)

Herpes zoster

Angular cheilitis

Recurrent oral ulceration

Papular pruritic eruptions

Seborrhoeic dermatitis

Fungal nail infections

Clinical stage 3

Unexplained severe weight loss (>10% of presumed or measured body weight)

Unexplained chronic diarrhea for longer than one month

Unexplained persistent fever (above 37.6°C intermittent or constant, for longer than one month)

Persistent oral candidiasis

Oral hairy leukoplakia

Pulmonary tuberculosis (current)

Severe bacterial infections (such as pneumonia, empyema, pyomyositis, bone or joint infection, meningitis or bacteraemia)

Acute necrotizing ulcerative stomatitis, gingivitis or periodontitis

Unexplained anaemia (<8g/dl), neutropaenia (<0.5 × 109 per litre)

Or chronic thrombocytopaenia (<50 × 109 per litre)

Clinical stage 4

HIV wasting syndrome

Pneumocystis pneumonia

Recurrent severe bacterial pneumonia

Chronic herpes simplex infection (orolabial, genital or anorectal of more than one month's

Duration or visceral at any site)

Oesophageal candidiasis (or candidiasis of trachea, bronchi or lungs)

Extrapulmonary tuberculosis

Kaposi’s sarcoma

Cytomegalovirus infection (retinitisn or infection of other organs)

Central nervous system toxoplasmosis

HIV encephalopathy

Extrapulmonary cryptococcos is including meningitis

Disseminated non-tuberculous mycobacterial infection

Progressive multifocal leukoen cephalopathy

Chronic cryptosporidiosis (with diarrhoed)

Chronic isosporiasis

Disseminated mycosis (coccidiomycosis or histoplasmosis)

Recurrent non-typhoidal Salmonella bacteraemia

Lymphoma (cerebral or B-cell non-Hodgkin) or other solid HIV-associated tumours

Invasive cervical carcinoma

Atypical disseminated leishmaniasis

Symptomatic HIV-associated nephropathy or

Symptomatic HIV-associated cardiomyopathy