PREDICTORS OF DEPRESSION AMONG PATIENTS SEEKING ANTIRETROVIRAL THERAPY (ARVS)

APPROACH: A CROSS-SECTIONAL STUDY AT FIVE UNITID TREATMENT CLINICS, UNIVERSITY STAFF HEALTH, KANGEMI, TIGONI, PUMWANI AND MAJENGO.

By

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A project submitted to the University of Nairobi Institute of Tropical and Infectious Diseases (UNITID) in partial fulfillment for the Degree of Masters of Science in Medical Statistics

(Msc MedStat)

INSTITUTE OF TROPICAL AND INFECTIOUS DISEASES (UNITID)

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Declaration

I the undersigned declare that this project is my original work and to the best of my knowledge has not been presented for the award of a degree in any other University.

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Dedication

This work is dedicated to My son Henry Oyugi Odia and my wife Olga Ogosi Otieno

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ABBREVIATIONS

AIDS	Acquired Immuno Deficiency Syndrome
ARV	Antiretroviral
CES-D	Centers for Epidemiologic Studies Depression scale
HAART	Highly Active Antiretroviral Therapy
HIV	Human Immunodeficiency Virus
KAIS	Kenya AIDS Indicator Survey
PLWHA	People Living With HIV AIDS
UNITID	University of Nairobi Institute of Tropical and Infectious Diseases

Abstract

The entire study was summarized below:

Objectives: To determine the prevalence of and factors associated with depression among patients seeking ARV's at UNITID treatment clinics.

Design: Cross-sectional study.

Participant and setting: Patients seeking ARVs at five UNITID treatment clinics, University staff health, Kangemi, Tigoni, Pumwani and Majengo.

Measurements: The primary outcome was symptoms of depression, as measured by Centers for Epidemiologic Studies Depression scale (CES-D). Multivariate logistic regression was used to identify the association of age, gender, symptoms and opportunistic infection related to HIV i.e. wasting, shingles, pneumonia, thrush, disclosure of HIV status to parent, spouse, child, relative, and friend, being affected with HIV, CD4 T lymphocytes versus depression.

Results: Among 159 patients, 49(30.8%) respondents screened positive for depression. Variables associated with depression in multivariate analysis included oral thrush adjusted odds ratio 2.57(95%: 1.08, 6.12), *p-value* = 0.032, Wasting, adjusted odds ratio 3.88(95%; 1.63-9.21), *p-value* = 0.002.

Conclusions: The prevalence of depression found in this study is an indicator that patients seeking ARVs are depressed. Oral thrush and wasting are the only factors associated with depression.

Chapter 1

1 Introduction

1.1 HIV burden and ARVs

An estimated 33.2 million people worldwide were living with HIV, 2.5 million became newly infected and 2.1 million lost their lives to AIDS by the end of 2007.[1] Sub Sahara Africa remains the worst affected region in the world. A little more than one-tenth of the world population lives in sub-Saharan Africa, yet it is home to almost 68% of all people living with HIV. [1] Highly Active Antiretroviral Therapy (HAART) was a breakthrough in the industrialized world, leading to reduction of mortality and the improvement of quality of life of People Living With HIV and AIDS (PLWHA).[2-3] In Kenya, more than 1.4 million people are living with HIV/AIDS. By June 2008, approximately 190,000 HIV-infected Kenyan adults were receiving ARVs.[4]

1.2 Depression and its impact

Twenty percent of the HIV infected patients experienced clinical depression, which is the most commonly, observed mental health disorder. [5-6] Depressive symptoms have been associated with risk behaviour, non- adherence to medications and shortened survival. [7-10] Failure to recognize depression may endanger both the patient and others in the community. Patients with depression are at higher risk of co-morbid psychiatric, alcohol, and substance use-related disorders, particularly those associated with alcohol, cannabis and cocaine use. Depression was shown to be a major problem among those on ARVs. The good news is that currently, there are medications used to manage depression. Diagnosis of clinical depression and its management

will lead to great benefit for those with HIV/AIDS and others in the community. Hence, improvement in quality and duration of life by reduction in risk behaviour and adherence to drugs.

1.3 The tool used for diagnosis of depression

There are various tools available for diagnosis of depression e.g. Beck Depression Inventory (BDI).The BDI consists of 21 items of which a total score is calculated. A score of > 13 is indicative of depression. The primary outcome of this study was depression, as measured by Center for Epidemiologic Studies Depression Scale(CES-D). This tool was developed by Center for Epidemiologic Studies, National Institute of Mental Health. Its internal consistency reliability (Cronbach's alpha) ranges from 0.84 to 0.90. The CES-D is designed to measure depressive symptoms in the general population (i.e. non-psychiatric persons older than 18). It measures the major components of depressive symptomatology, including depressive mood, feelings of guilt and worthlessness, psychomotor retardation, loss of appetite, and sleep disturbance. In another study where CES-D was used Cronbach's coefficient alpha in the study was 0.87.[29] CES-D is 20-item self-report measure for depression. Subjects rate the degree to which they have experienced a range of symptoms of depression on items such as "I had crying spells" or "I felt lonely". Items 4,8,12 and 16 were assigned weights **3**- Rarely or none of the time to **0**-All of the time. All the other items were assigned **0**-Rarely or none of the time to **3**-All of the time *(Appendix1).* The score range from 0 to 60, with higher scores indicating greater depressive symptoms. It should be noted that asking the patient a simple and direct question such as, "Are you depressed?" will not provide a better diagnostic criteria of depression. A patient with a score of ≥16 was considered to have clinically depressive symptoms. Those who had scores between 16-26 were considered

moderate depressive symptoms while those with 27 scores and above were considered to have severely depressive symptoms.

1.4 Motivating Study

This cross sectional study was part of a larger two-year prospective study on predictors of adherence to ARVs. So far there are no published data on prevalence of and factors associated with depression among patients seeking ARVs in Kenya. Identification of factors associated with depression in relation to HIV and continued use of ARVs will facilitate introduction of appropriate treatment procedures leading to faster healing of the patients. The application of Logistic regression the analysis enabled the identification of the risks associated with depression.

1.4.1 Sampling

In order to carry out the study, patients presented themselves at five UNITID treatment clinics; University staff health, Kangemi, Tigoni, Pumwani and Majengo, were enrolled. Before enrollment they consented, then screened for study eligibility. Further counseling was offered to those that had made a decision to start on HAART. Enrollment occurred over a two-year period with follow-up duration of one year. For the purpose of this project, UNITID availed data for the first 159 subjects only.

1.4.2 Inclusion and exclusion criteria

Inclusion criteria were as follows:

- Patients above 18 years of age and below 60 years.
- HIV infected, willing to start on ARVs.
- Gave informed consent to participate.

- Have CD4 T lymphocyte count of ≤ 200.
- Normal liver function test result

Exclusion

Patients who did not meet any one of the above set criteria were excluded.

1.4.3 Ethical approval

The main protocol on the factors associated with depression among patients on ARVs was approved by the ethics review board of Kenyatta National Hospital, Kenya.

1.4.4 Study procedure

Patients who attended any of the five treatment clinics and were willing to participate in the study were welcomed by the receptionist. Specific informed consent for the study was sought and information about the study procedures, participation, risks and potential benefits were provided and explained by the study nurse. They were interviewed by a research assistant using standardized questionnaire and administered in a private area. In addition to the identification information, next of kin, physical address and contact details, the baseline study questionnaire for all patients covered socio-demographics, HIV history and depression status using the CES-D instrument.

1.5 Objective of the study

The main objective for this study is to determine the predictors of depression among HIV positive patients on ARVs.

1.5.1 Specific objectives

The following were the specific objectives;

1. To determine the prevalence of depression among HIV positive patients seeking ARVs.
2. To establish association between depression and demographic factors.
3. To determine the factors associated with depression using multivariate logistic regression.

Study design

The study was based data that was collected Cross-sectionally at five UNITID treatment clinic.

Sample size

For the main study, the formula below was applied to calculate sample size. The Standard normal deviate at α=0.05 level of significance was $Z_{1-\alpha/2} = 1.96$, p = the prevalence of depression at 36% and d= the margin of error of 5%. Calculated n= 354. For this project, data was available for 159 patients.

The formula is

$$n = \frac{(p)(1-p)(Z_{1-\alpha/2})^2}{d^2}$$

Chapter 2

2 Literature Review

2.1 Prevalence of and factors associated with depression

Depression is atleast 3 times as likely among individuals with HIV compared with the general population, with prevalence estimates of 36% to 37% of HIV-infected individuals. [11,12] Depression has been linked with poor functional status [13] and the necessity of third-party assistance in activities of daily living, like bill paying by a representative payee. [14] It is also associated with poor health, decreased antiretroviral (ARV) adherence, and more rapid progression to AIDS and death among people with HIV in the United States. [15-19] Depression is one of the predictors of non adherence to ARV, with the prevalence of 55.8%. [30] The impact of depression on HIV outcomes is exacerbated by the fact that mental services are significantly underutilized among individuals with HIV. [20] Treating depression in HIV infected individuals is associated with improved ARV utilization and adherence. [21] Being white, having a representative payee, heavy alcohol consumption, and recently missed medical appointment were associated with depression. [22]

In Belo Horizote (Brazil), a study was carried out using logistic regression to assess the prevalence and factors associated with anxiety and depression on 386 who received their first anti-retroviral prescription. The prevalence of moderate to severe anxiety and depression were 35.8% to 21.8% respectively. Female gender, low schooling, lack of health insurance, attendance to psychotherapy, difficulty in accessing health services and exposure category were

independently associated with anxiety using logistic regression. On the other hand, female gender, lack of health insurance, low income, living alone, and lacking sexual partner in the last month were independently associated with depression. [23] Using logistic regression a study established that social support, major life stress and HIV related symptomatology were significantly associated with depression. Length of time since seropositive notification was not significantly associated with depression. [24]

High levels of depression was predicted by lower perceived social support, attributions that health was influenced more by chance, high-risk sexual behavior practices, and greater number of HIV illness symptoms and greater duration of time knowing of one's own positive serostatus The study used logistic regression. [25] HIV clinical status, lack of emotional support and higher plasma viral load among 120 HIV infected women (in Brazil), were associated with depression. [26] In Denmark, 205 HIV positive patients were included in a questionnaire based study. The aim of the study was to investigate the prevalence of depression in out-patient clinic and to detect factors of importance for the development of depression. Self-reported stress, loneliness, constant thought about HIV and being in a difficult financial situation were associated with the risk of depression. [27]

A study amongst HIV infected women found that depressive symptoms is significantly associated with frequency of reading spiritual or religious materials (p=0.02). Of the women who reported reading spiritual or religious materials "daily" or "almost every day" (n=91), only 27% (n=12) had high depressive symptoms. Of the 7 women who reported that they "never" or rarely read spiritual or religious materials, 71% (n=5) had higher depressive symptoms. [28]

2.2 Justification of the study

Several measures for example availability of ARVs, support groups, counseling services have been put in place for HIV positive patients. Knowing the prevalence and factors associated with depression will help develop, remedies for high level of depression and measures that will help reduce depression among patients seeking ARVs to bear minimum. These will help improve level of adherence leading to patients living longer and better life. In Kenya, there is no published data showing the prevalence and or factors associated with depression in HIV infected individuals on antiretroviral therapy.

2.3 Research Question

This project is meant to answer the following questions:-

What is the prevalence of depression among HIV positive patients seeking ARVs?

What are the predictors of depression among HIV positive patients seeking ARVs?

2.4 Research Hypothesis

There are a number of hypotheses to be tested. Several factors are suspected to be associated with depression among HIV positive patients seeking. These factors will be tested for significance of association. The main hypothesis to be tested is:

Null hypothesis (H_o)

There is no association between factors and having depression. The association will assessed by Wald test in logistic regression. Odds ratio was used to show magnitude of association.

$$H_o = \beta_1 = \cdots \beta_k = 0$$

Alternative hypothesis (H_1)

There is an association between factors and having depression.

H_1: *Not all* $\beta_i = 0$

Chapter 3

3 Methods of Analysis

3.1 Structure of the data

The response variable was depression which had two outcomes i.e. 0= No and 1= Yes. The explanatory variables gender (0= Female, 1=Male), wasting, shingles, thrush, pneumonia, parent, spouse, child, friend, relative and being affected with HIV/AIDS are all categorical with answer of 0= No and 1= Yes. The other explanatory variables are numeric, age and CD4 T lymphocytes. The response variable and explanatory variables made it appropriate to use stepwise logistic regression. Logistic regression is one of the methodologies that allow us to fit a model. The information stated below explains further the use of this methodology from statistical modeling.

3.1.1 Main ideas of statistical Modeling

The procedures stated here provided a clear guideline on the steps followed in statistical modeling. Modeling process involves four steps:-

1. Specifying model in two parts: equations linking the response and explanatory variable and the probability distribution of the response variable.
2. Estimating parameters used in the model.
3. Checking how well the model fit the actual data.
4. Making inferences: for example, calculating confidence intervals and testing hypotheses about the parameters.

Before applying any statistical modeling, we must use appropriate methodology. The table below shows major methods of statistical analysis. It also confirms that based on the data types for this study logistic regression was appropriate.

Table 3.1 Major methods of statistical analysis

Response	**Explanatory variables**	**Methods**
Continuous	Binary	t-test
	Nominal,>2 categories	Analysis of variance(ANOVA)
	Ordinal	Analysis of variance(ANOVA)
	Continuous	Multiple Regression
	Nominal and continuous	Analysis of covariance(ANCOVA)
		Multiple Regression
Binary	Categorical	Contingency tables, Logistic regression
	Continuous	Logistic, probit
	Categorical and continuous	Logistic regression
Nominal with >2 categories	Nominal	Contingency tables
	Categorical and continuous	Nominal logistic regression
Ordinal	Categorical and continuous	Ordinal logistic regression
Counts	Categorical	Log-linear models
	Categorical and continuous	Poisson regression
Failure times	Categorical and continuous	Survival analysis
Correlated responses	Categorical and continuous	Generalized estimating Multilevel

3.1.2 Generalized Linear Models (GLM)

One of the most important developments in statistical theory over the past several decades has been broadening of linear models from classic $Y = \alpha + \beta_1 X_1 + ... + \beta_n X_n + \varepsilon$ (with conditional probability density P(Y|X)) to encompass much more diverse class of probabilistic distributions. Generalized Linear Models are abroad class of models predicting the outcome as a response function of some linear combination of a set of predictors. To define a GLM, you need to choose:

a) A link function relating the linear predictor to the predicted mean of the response

b) A function defining the "noise" or "error" probability distribution around that mean.

Genaralizing the classic linear model

The classic linear model

$$Y = \alpha + \beta_1 X_1 + ... + \beta_n X_n + \varepsilon \qquad (1).$$

The right hand side of equation (1) has two components: a deterministic component determining the *predicted mean* $\alpha + \beta_1 X_1 + ... + \beta_n X_n$ and a stochastic component expressing the *noise distribution* around the mean $\varepsilon \sim N(0, \delta^2)$.

The following steps are for defining a GLM;

Step 1: Break the two components apart and specify a more indirect functional relationship between them.

For any particular set of predictor variables $\{X_i\}$, there is a predicted mean μ. The probability distribution on the response Y is a function of that μ.

$$Y = \mu + \varepsilon \tag{2}$$

$$p(Y = y;\mu) = \frac{1}{\sqrt{2\pi\delta^2}} \exp \frac{-(y-\mu)^2}{\delta^2} \tag{3}$$

By choosing other functions to map from μ to *p(y)* we can get to other probability distributions.

Step 2: We loosen the relationship between the predicted mean and the predictor variables.

In the classic linear model of equation (1), the predicted mean was a linear combination of the predictor variables. In generalized linear model, we call this linear combination η and allow the predicted mean to be an invertible function of η. η is the *linear predictor*. The function relating μ to η is called the *link function*. In classic linear regression, the link function is the identity function, so that η= μ.

3.1.3 Logistic Regression as a Generalized Linear model

We want a GLM that models binomially distributed data from *n* trails. Instead of viewing the response as the number of successful trials *r* we view the response as the proportion of successful trials $\frac{r}{n}$ let this be called Y. Now the mean number of successes for a binomial distribution is *pn;* hence the mean proportion is *p*. *p* is the predicted mean μ of our GLM. The resulting model is

$$P(Y = y; p) = \binom{n}{y} p^y (1-p)^{(n-y)} \tag{4}.$$

This is choosing the distribution on Y given the mean *p*, which is the binomial GLM family.

Choosing a relationship between the linear predictor η and the mean p; Unlike the case with the classical linear model, the identity link function is not a possibility, because η can potentially be any real number, whereas the mean proportion p of successes can only vary between 0 and 1. For binary response, the link function is the LOGIT given by

$$\log\left(\frac{p}{1-p}\right)=\eta. \tag{5}$$

It follows therefore that the probability of success is

$$p=\frac{e^{\eta}}{1+e^{\eta}}. \tag{6}$$

Logistic Regression model

In logistic regression, we model the natural logs of ODDS of an event. From equation (5), we have natural ODDS of an event. This equation shows that the link function for logistic regression is **logit**. For example here the response of interest was binary that depression yes or no.

Let p = P(Y=1) i.e. success or depression.

1- p = P(Y=0) i.e. failure or no depression.

Then ODDS of an event is $\left(\frac{p}{1-,p}\right)$ and the **logit** is $\log\left(\frac{p}{1-p}\right)$.

Like in linear models, we have simple and multiple regression. The same applies to logistic regression i.e. we have simple logistic regression and multiple logistic regression. The sections that follow show the various models for logistic regression.

3.1.4 Simple Logistic regression model

Simple logistic regression model is of the form;

$$\log_e\left(\frac{p_i}{1-p_i}\right) = \beta_0 + \beta_1 X_i \qquad (7)$$

β_0 and β_1 are unknown parameters to be estimated.

The primary interest is in estimating and testing hypotheses regarding β_1. We used Wald test for test of hypothesis. The Large-Sample test (Wald Test) is carried out as follows:

Hypothesis

H_0: $\beta_1 = 0$ $\quad$ H_A: $\beta_1 \neq 0$

Calculated Wald

$$T.S.: \chi^2_{obs} = \left(\frac{\hat{\beta}_1}{\hat{\sigma}_{\hat{\beta}_1}}\right)^2 \qquad (8)$$

$$R.R.: \chi^2_{obs} \geq \chi^2_{\alpha,1}$$

$$P-val: P(\chi^2 \geq X^2_{obs})$$

Note :T.S = Test Statistic and R.R = Rejection Region

Decision: We reject the null hypothesis is $\chi^2_{obs} > \chi^2_{\alpha,1}$

Interpretation of β_1

After testing the hypothesis, the next step is interpretation. In this section, we describe how to interpret the parameters of the logistic regression model.

We interpret $\exp(\beta_1)$ as the ODDS (or change in risk compared to **unity**). The Odds Ratio is defined as

$$(OR)= \exp(\beta_i)= e^{\beta_1}. \quad (9)$$

Suppose X is a continuous variable (e.g. Age), then $\exp(\beta_1)$ is the change in risk for every additional year of age.

Suppose X is categorical (e.g Gender), then $\exp(\beta_1)$ is an ODDS ratio of one group to the other, which compares their ODDS of event e.g ODDS for males relative to females.

Inferences on β_1 and Odds Ratio

The next step after interpreting the meaning of the coefficients is statistical inference. In making inference odds ratio is used. That is e^{β} represents the change in the odds of the outcome (multiplicatively) by increasing x by 1 unit. If $\beta = 0$, the odds and probability are the same at all x levels ($e^{\beta} =1$), if $\beta > 0$, the odds and probability increase as x increases ($e^{\beta} >1$) and if $\beta < 0$, the odds and probability decrease as x increases ($e^{\beta} <1$)

Constructing 95% Confidence Interval for Odds Ratio

The following steps are used when constructing 95%CI for Odds Ratio

Step 1: Construct a 95% CI for β

$$\hat{\beta} \pm 1.96\hat{\sigma}_{\hat{\beta}} \equiv \left(\hat{\beta}-1.96\hat{\sigma}_{\hat{\beta}}, \hat{\beta}+1.96\hat{\sigma}_{\hat{\beta}}\right) \quad (10)$$

Step 2: Raise $e = 2.718$ to the lower and upper bounds of the CI:

$$\left(e^{\hat{\beta}-1.96\hat{\sigma}_{\hat{\beta}}}, e^{\hat{\beta}+1.96\hat{\sigma}_{\hat{\beta}}}\right) \quad (11)$$

If entire interval is above 1, conclude positive association, if entire interval is below 1, conclude negative association and if interval contains 1, cannot conclude there is an association.

3.1.5 Logistic regression prediction

The predicted probability of depression was estimated using:

a) Simple logistic regression

$$\hat{p} = \frac{\exp(\hat{\beta}_0 + \hat{\beta}_1 X)}{1 + \exp(\hat{\beta}_0 + \hat{\beta}_1 X)} \tag{12}$$

b) Multiple logistic regression

$$\hat{p} = \frac{\exp(\hat{\beta}_0 + \hat{\beta}_1 X_1 + ... + \hat{\beta}_k X_k)}{1 + \exp(\hat{\beta}_0 + \hat{\beta}_1 X_1 + ... + \hat{\beta}_k X_k)} \tag{13}$$

Adjusted Odds ratio for raising x_i by 1 unit, holding all other predictors constant:

$$OR_i = e^{\beta_i}$$

3.1.6 Multiple Logistic Regression

For multiple Logistic Regression model there are more than one explanatory variable. The formula is

$$\log_e\left(\frac{p}{1-p}\right) = \beta_0 + \beta_1 X_{1i} + ... + \beta_k X_{ki} \tag{14}$$

Where $X_1, X_2, \ldots, X_k$ are the explanatory variables and

$\beta_0, \beta_1, \ldots, \beta_k$ are the unknown regression parameters.

3.2 Models to establish the factors

There is need to establish the best-fitted model. That is the model with predictors of depression. The model fitted was of the form

$$\text{Log(odds)} = \alpha + \beta_1 x_1 + \ldots + \beta_k x_k$$

The explanatory variables x_i were used to fit the best model are age, gender, wasting, pneumonia, oral thrush, shingles, CD4 T lymphocytes, disclosure of HIV status to parent, spouse, friend, relative, child and being affected with HIV/AIDS.

3.2.1 Testing overall model

Before we carry model fitting we need to

a) Ask the question
   - Does model including given independent variable provide more information about dependent variable than model without this variable?

b) Know the three tests used to identify the fit
   - Likelihood ratio statistic (LRS)
   - Hosmer-Lemeshow statistic

1. Likekihood Ratio test

Just as in analysis of variance, we are often interested in conducting tests of hypothesis that introducing several model parameters simultaneously leads to a better overall model. In this case we cannot simply use a single Wald statistic for hypothesis testing. Instead, the most common approach is to use the LIKELIHOOD-RATIO TEST. A generalized linear model assigns a likelihood to its data as follows:-

$$Lik(\vec{x};\hat{\theta}) = \prod_i P(x_i \mid \hat{\theta}) \qquad (15)$$

Now suppose that we have two classes of models, M_o and M_1, and M_o is nested inside M_1 (that is, the class M_o is a "special case" of the class M_1). It turns out that if the data are generated from a model M_o is the correct model, the ratio of the data likelihoods are in the Maximum Likelihood estimates for M_o and M_1 is well behaved. In particular, twice the log of the likelihood ratio is distributed as a χ^2 random variable with degrees of freedom equal to the difference k in the number of free parameters in the two models. This quantity is sometimes called the DEVIANCE:

$$2\log\frac{Lik_{M_1}(\vec{x})}{Lik_{M_0}(\vec{x})} = 2[\log Lik_{M_1}(\vec{x}) - \log Lik_{M_0}(\vec{x})] \sim \chi^2_k \qquad (16)$$

Decision

The model is of good fit if $\chi^2_{obs} > \chi^2_{Table}$ That is the model is of good fit if *p-value*<0.05.

2. **Hosmer-Lemeshow**

This is another measure of lack of model fit. Hosmer and Lemeshow recommend partitioning the observations into 10 equal sized groups according to their predicted probabilities. Then

$$G^2_{HL} = \sum_{j=1}^{10}\frac{(O_j - E_j)^2}{E_j(1 - E_j/n_j)} \sim \chi^2_8 \qquad (17)$$

where

n_j = Number of observations in the j^{th} group

O_j = $\sum_i y_{ij}$ = Observed number of cases in the j^{th} group

E_j = $\sum_i \hat{p}_{ij}$ = Expected number of cases in the j^{th} group

Decision

There is model lacks fit if $\chi^2_{obs} > \chi^2_{Table}$. That is the model is of poor fit if *p-value*<0.05.

Sensitivity and specificity

Sensitivity = P(correct prediction | event did occur)

= P(predict depression | subject has depression)

Specificity = P (correct prediction | event didn't occur)

= P (predict no depression | subject has no depression)

False positive rate = P (incorrect prediction | predicted occurrence)

= P (subject has no depression | predicted depression)

False negative rate = P (incorrect prediction | predicted no depression)

= P (subject has depression | we predicted depression)

3.2.2 Application of exploratory stepwise logistic regression

In this data set for each participant, there is one measurement for the outcome variable: depression or no depression by pneumonia, shingles, oral thrush and wasting, disclosure HIV status to parent, spouse, child, friend and relative and someone close dying of HIV/AIDS.

Forward eliminations step

Stepwise regression was performed through two stages.

Step 1: In the first stage, a logistic regression will be fit between the outcome variable and each of the covariables in turn to identify which are most likely to be correlated to the outcome.

Decision: Choose the variable, say variable 1, with the smallest p-value and whose magnitude <0.25 which is called the entry p-value (Hosmer and Lemeshow).

Step 2: Fit the model containing Variable 1 and each other of the variables in turn.

Decision: Choose the variable, say variable 2, which in combination with Variable 1 gives the smallest p-value < 0.25 in the two variate regression.

Step 3: Fit the model containing Variables 1,2 and each other variable in turn.

Decision: Choose the variable which in combination with variables 1,2, gives the smallest p-value in the three variate regression, say Variable 3.

Backward eliminations step: Three or more variate models will include a backward elimination step in which the variable is kept only if it improves the model by a threshold value i.e. if the pvalue of the model without the value, exceeds the threshold elimination p-value denoted by PR, say 0.30((Hosmer and Lemeshow).

Step 3 is repeated until the last step which occurs when all the variables which are significant according to the entry and elimination p-values, PE and PR.

3.2.3 Statistical analysis plan

The data collected from the respondents were cleaned, coded, and analyzed using SPSS 17.0 for windows. The analysis consisted basic summary of patients characteristics and univariate analysis of the relation between depression and various factors.

Step1: Data summaries: Frequencies, mean, standard deviation, median, minimum and maximum will be used appropriately.

Step2: Exploratory modeling: The relationship of potential covariates to depression outcome variables will be explored. This will be done through stepwise logistic regression inorder to choose the most explanatory covariables in the data set.

Step 3: Logistic Regression Modeling: A logistic regression model will be fit between depression outcome measurement and the covariables in step 2. Diagnostic procedures will be used in this model to determine any influential measurements.

3.2.4 Data Variables

DEFINITION OF OUTCOME MEASUREMENTS		
Data	**Question/Variable**	**Type/Codes**
Demographic	Age	Continuous/Years
	Gender	0=Female 1=Male
Who have you told about your HIV status? Disclosure	Spouse(ftspousehiv)	0= No 1= Yes
	Children(ftchildhiv)	
	Parents or siblings(ftpshiv)	
	Other relatives or friends(ftrelfhiv)	
	Friends(ftfrienhiv)	
Being affected with HIV	Lost closest person to HIV(fclosthiv)	0= No 1= Yes
Symptoms or opportunistic infections related to HIV/AIDS	CD4 T lymphocytes	Count
	Wasting(foiwating)	0= No 1= Yes
	Shingles(foishing)	
	Pneumonia(foipneum)	
	Cancer(foicancer)	
	Thrush(foithrush)	
Depression	Depression	0= No 1= Yes

Chapter 4

4 RESULTS

This chapter reports on the findings of the project. The results are presented beginning with descriptive statistics, univariate analysis and finally multivariate analysis.

4.1 Descriptive Statistics

It is evident that majority of patients seeking ARVs are female (83%). Female to male ratio was 5:1. Average age was 36.5(8.5) years with median of 35 years. The youngest was 19 years and maximum age of 59 years. Table 4.1

Table 4.1: Demographic characteristics

Characteristic	**Number n =159**	**Percent (%)**
Gender Male	27	17
Female	132	83
Age in years	**Mean(SD)**	**Median(Min-Max)**
	36. 8(8.2)	35(19-59)

Equal proportion (42.8%) had wasting or oral thrush, 40.3% had pneumonia. Those that had shingles were 25.8%, while only 0.6% had cancer. Mean CD4 T lymphocytes was 80(47.6) with the median of 70 counts. The lowest count was 20 and the highest was 300. Table 4.2

Table 4.2 :Clinical markers

Characteristic	Number n =159	Percent (%)
Opportunistic infections		
Wasting	68	42.8
Thrush	68	42.8
Pneumonia	64	40.3
Shingles	41	25.8
Cancer	1	0.6
CD4 T lymphocytes counts (n=115)	**Mean(SD)** 80(47.6)	**Median(Min-Max)** 70(20-300)

39.6% had disclosed their HIV status to parent, 34% to parent , 32.7% to spouse, 23.9% had disclosed their status to their relative while only 14.5% had disclosed to their child. More than half, 59.7% had someone close dying of AIDS related diseases. Table 4.3

Table 4.3: Psychosocial characteristics

Characteristic	Number n =159	Percent (%)
HIV status disclosure to		
Parent	63	39.6
Friend	54	34.0
Spouse	52	32.7
Relatives	38	23.9
Child	23	14.5
Someone close died of HIV/AIDS	95	59.7

4.2 Prevalence of depression

The prevalence of depression was 30.8%, with 95% CI 23.6% to 38%.

Average age for males was 40.2 years compared to mean of 35.8 years for females. This difference is statistically significant *p-value* 0.04. Males had higher mean CD4, 92.8 counts compared to females mean CD4 of 77.6 counts. This difference in mean CD4 counts was statistically significant, *p-value* 0.04. Table 4.4

4.4 Comparison of mean Age, CD4 T lymphocytes by gender

Characteristic	**Male**	**Female**	**p-value**
	Mean(SD)	**Mean(SD)**	
Age in years	40.2(10.2)	35.8((7,9)	0.04
CD4 T Lymphocytes	92.8(57.3)	77.6(45.5)	0.21

4.3 Univariate analysis

In univariate analysis, gender, opportunistic infections like pneumonia and shingles, disclosure HIV status to parent, spouse, child, friend and relative and someone close dying of HIV/AIDS were not associated with depression. Oral thrush and wasting were associated with depression. For oral thrush, the odds ratio was 2.33(95%: 1.18, 4.64), *p-value* =0.01. Patients with oral thrush were 2.33 times likely to develop depression than those without oral thrush. For wasting the odds ratio, 2.33(95%: 1.18, 4.64), *p-value* =0.01. Patients who had wasting were 2.33 times likely to have depression compared to those who did not have wasting. Table 4.5.

The mean difference in age and CD4 T lymphocytes counts for those depressed and non depressed was not statistically significant. However, those that had depression were younger than those who did not have. Those depressed had higher mean CD4 counts compared to those not depressed. Table 4.6.

Table 4.5: Univariate analysis

Characteristic	Depression		O.R (95%C.I)	P value
	Yes(%)	No(%)		
Gender Male	7(25.9)	20(74.1)	0.75(0.29-1.91)	0.55
Female	42(31.8)	90(68.2)		
Opportunistic infections				
Wasting	28(41.2)	40(58.8)	2.33(1.18-4.64)	0.01*
Shingles	16(39)	25(61)	1.65(0.78-3.47)	0.19
Pneumonia	24(37.5)	40(62.5)	1.68(0.85-3.38)	0.13
Thrush	28(41.2)	40(58.8)	2.33(1.18-4.64)	0.01*
HIV status disclosure to				
Parent	18(28.6)	45(71.4)	0.84(0.42-1.68)	0.62
Spouse	15(28.8)	37(71.2)	0.87(0.42-1.80)	0.71
Child	9(39.1)	14(60.9)	1.54(0.62-3.85)	0.35
Friend	19(35.2)	35(64.8)	1.36(0.67-2.74)	0.39
Other relatives	14(36.8)	24(63.2)	1.43(0.67-3.09)	0.36
Someone close died of HIV/AIDS	34(35.8)	61(64.2)	1.82(0.89-3.72)	0.09

**significant p<0.05*

4.6 Comparison of mean Age, CD4 T lymphocytes by depression

Characteristic	Depression		p-value
	Yes	No	
	Mean(SD)	Mean(SD)	
Age in years	35.7(7.9)	36.9((8.7)	0.39
CD4 T Lymphocytes	85(44.5)	77.5(49.2)	0.43

4.4 Multivariate analysis

After carrying out stepwise multiple logistic regressions, having oral thrush and wasting were independently statistically significant. For oral thrush, the adjusted odds ratio 2.57(95%: 1.08, 6.12), *p-value* = 0.032. Those who had oral thrush were 2.57 times likely to be depressed than those who did not have. For wasting, the adjusted odds ratio 3.88(95%; 1.63-9.21), *p-value* = 0.002. Patients who had wasting were 3.88 times likely to have depression compared to those who were not wasted. Table 4.7.

The final model fitted was

Model 1

Ln(odds)= -1.35 + 1.23*Wasting

-2LogLikelihood =134.668

Model 2

Ln(odds)= -2.06 + 1.36*Wasting + 0.90*Shingles + 0.95*Oral thrush

-2LogLikelihood =127.398

Model fit. The drop in -2LL = 16 = Model χ^2, df = 3, *p-value* =0.001. The model fit is significant.

Hosmer and Lemeshow test

Hosmer and Lemeshow confirms that model 2 is of the best fit with $\chi^2 = 2.098$ df = 5, *p-value* =0.84.

The overall prediction for the model is 64%, with sensitivity of 67.6% and specificity of 62.3%. False positive is 20% while false negative is 53.7%.

Table 4.7: Fitted Model of predictors of depression

Predictor	B	S.E	Wald	p value	O.R (95% C.I.)
Wasting	1.355	0.441	9.441	0.002**	3.88(1.63-9.21)
Shingles	0.902	0.504	3.204	0.073	2.46(0.92-6.62)
Oral thrush	0.945	0.442	4.575	0.032*	2.57(1.08-6.12)
Constant	-2.057	0.439	21.95	0.000	0.128

** *Significant* $p<0.01$ * *Significant* $p<0.05$

Chapter 5

5 Discussion and Conclusion

Among patients seeking ARVs at UNITID treatment clinics, we found the prevalence of depression to be 30.8%(95%CI: 23.6%, 38.0%). This finding is close to what has been published elsewhere. A study which used a similar tool (CESD) to measure depression but among HIV positive patients, found the prevalence of depression to be between 36% to 37%. [11,12] From this, we it shows clearly that there is depression among patients seeking ARVs.

Age and gender are not were not associated with depression. Other studies have shown that female gender associated with having depression. [23] In our case even though 31.8% of female were depressed compared to 25.9% of male, this was not statistically significant *p-value* =0.55. Hence, female gender is not a risk factor associated with depression.

In order to determine factor that are independently associated with depression, a stepwise logistic regression was used to fit the model. Opportunistic infections like pneumonia and shingles, disclosure HIV status to parent, spouse, child, friend and relative and someone close dying of HIV/AIDS were not associated with depression. Oral thrush and wasting were independently statistically significant. For oral thrush, the adjusted odds ratio 2.57(95%: 1.08, 6.12), *p-value* = 0.032. Those who had oral thrush were 2.57 times likely to be depressed than those who did not have. For wasting, the adjusted odds ratio 3.88(95%; 1.63-9.21), *p-value* = 0.002. Patients who had wasting were 3.88 times likely to have depression compared to those who were not wasted

5.2 Conclusion and Recommendation

The prevalence of depression found in this study is an indicator that patients seeking ARVs are depressed. Oral thrush and wasting are the only factors associated with depression. Appropriate intervention e.g. use of antidepressants should be in place. Management of oral thrush and wasting needs to be intensified.

5.3 Shortcomings of this study

These are some of the shortcomings of the study. One, explanatory variables like marital status, income level, number of children among others should have been availed. Two, there is need to use much bigger study.

5.4 Further work

There is need for prospective study to determine the level of adherence to ARVs, association between depression and adherence and whether there is reduction in depression with time.

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Appendix I

Center for Epidemiologic Studies Depression Scale (CES-D)

Below is a list of some of the ways you may have felt or behaved. Please indicate how often you have felt this way during the **past week**:(Circle one number on each line).

During the past week....	**Rarely or none of the time** (< 1day)	**Some or a little of the time** (1-2 days)	**Occasionally or a moderate a mount of time** (3-4 days)	**All of the time** (5-7 days)
1.I was bothered by things that usually don't bother me	0	1	2	3
2.I did not feel like eating; my appetite was poor	0	1	2	3
3.I felt like I could not shake of blues even with help from my family	0	1	2	3
4.I felt that I was just good as other people	3	2	1	0
5.I had trouble keeping my mind on what I was doing	0	1	2	3
6.I felt depressed	0	1	2	3
7.I felt that everything I did was an effort	0	1	2	3
8.I felt hopeful about the future	3	2	1	0
9.I thought my life had been a failure	0	1	2	3
10.I felt fearful	0	1	2	3
11.My sleep was restless	0	1	2	3
12.I was happy	3	2	1	0
13.I talked less than usual	0	1	2	3
14.I felt lonely	0	1	2	3
15.People were unfriendly	0	1	2	3
16.I enjoyed life	3	2	1	0
17.I had crying spells	0	1	2	3
18.I felt sad	0	1	2	3
19.I felt that people disliked me	0	1	2	3
20.I could not "get going"	0	1	2	3