MODELLING THE FACTORS INFLUENCING WILLINGNESS TO PARTICIPATE IN HIV-1 VACCINE AND MICROBICIDE TRIAL: A CASE STUDYOF MATHARE PERI-NATAL CITY COUNCIL CLINIC

By

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Declaration

I, hereby declare that this Project is my original work and has not been presented for a degree in any other University.

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Dedication

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Abstract

The study evaluates the suitability of women participating in perinatal HIV-1 prevention program for HIV-1 vaccine and microbicide trials, willingness to participate in trials and knowledge of current performance of vaccines in in general and the future HIV vaccine performance. Follow-up among HIV-1 uninfected women after delivery was done for a a period of upto 1 year.

Using participants in perinatal HIV-1 prevention trials for vaccine and microbicide studies possed several advantages as it provides an adquate infrastructure and easy follow-up, its a high-risk cohort (group) and that women participating in Prevention of Mother-To-Child Transmission programs are more representative of reproductive birth giving cohort with a higher risk of infection.

The study entails finding a suitable odered logistic regression model which relates willingness to the factors influencing it and responses on willingness were utilized in predicting a sub-set of participants likely to be involved in the uptake and the subsequent participation of vaccine/microbicides vaccine.

At enrollment a total of 797 participants were interviewed and their willingness to participate was assessed through a face-to-face questionnaire and a follow-up for upto 1 year done. There was consistently high knowledge on the HIV prevention methods among the study participants. However, knowledge on vaccines in general and on future HIV vaccines was relatively low. Willingness to participate in the HIV vaccines was very high ($> 80\%$) of the study participants citing willingness to participant in HIV vaccine trials over the follow-up period.

On running an Ordered regression model, effectiveness and side-effects of the current vaccines were significant in modelling willingness to participate in the vaccine trials. The performance of the current vaccines is still key to future vaccine developments and their side-effects need to be minimized for better results and enhanced participation in future vaccine trials.

Abbreviations

AIDS	:	Acquired Immune Deficiency Syndrome
ANC	:	Anti-Natal Clinic
CI	:	Confidence Interval
CSWs	:	Commercial Sex Workers
HIV	:	Human Immune Virus
MoA	:	Ministry of Agriculture
NACC	:	National AIDS Countrol Council
OR	:	Odds Ratio
PMTCT	:	Prevention of Mother To Child Transmission
UPDF	:	Uganda People Defense Forces
SA	:	South Africa
KSH	:	Kenya Shilling
USA	:	United States of America
VPS	:	Vaccine Preparedness Study
WHO	:	World Health Organization
WTP	:	Willingness To Participate

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Chapter 1

Introduction

1.1 Background

HIV/AIDS has remained a major challenge in the world with a total of approximately 39.9 million (34.1 - 47.1 million) people living with the epidemic by the close of 2006. This represents an inceasing trend of about 12.0% compared to the 2004 statisticts by World Health Organization (WHO). Of this adults represented 37.2 million (32.1 - 44.5 million), women at 17.7 million (15.1 - 20.9 million) and children under 5 years at 2.3 million (1.7 - 3.5 million)[1]. The new infections stood at 5 million and deaths due to the disease was at 4.3 million (3.6 - 6.6 million) cases as at 2006. In the same year it was estimated that the new infections was 14,000 cases per day, with 95% from the developing countries. About 12,000 persons aged between 15 and 49 years of whom almost 50% were women and about 50% were between 15 and 49 years old. In many regions of the world, new HIV infections are heavily concentrated among young people (15 to 24 years of age), accounting for 40% of the total new HIV infections in 2006.

Sub-Saharan Africa continues to bear the brunt of the global epidemic. Two thirds (63%) of all adults and children with HIV, globally live in Sub-Saharan Africa with its epi-centre in Southern Africa. One third (32%) of all people with HIV globally live in Southern Africa and 34% of all deaths due to AIDS in 2006 occurred there. Of these, adults and children living with HIV/AIDs stood at 24.7 million (21.8 - 27.7 million) with 2.8 million (2.4 - 3.2 million) in the same groups respectively. The prevalence of HIV for the adults stood at 5.9% (5.2 - 6.7%) up

[1]The ranges are based on the best available information by the WHO, December 2006 AIDs Update

from 6.0% in 2004. Adults and children deaths due to AIDs in 2006 was 2.1 million (1.8 - 2.8 million) in 2006 from 1.9 million (1.7 - 2.3 million) in 2004.

In Kenya, the government declared HIV/AIDS a national disaster in 1999 and a national campaign targeting prevention, care and treatment initiated. According to the Kenya AIDS Indicator Survey 2007, the national HIV prevalence rates was estimated at 7.1%.

Current preventive efforts to stem the spread of the global HIV/AIDS epidemic [2] have been largely unsuccessful and an effective HIV-1 [3] vaccine[4] or microbicide, a female controlled preventive method is urgently needed. Promising HIV-1 vaccines and microbicides that have been developed are in various stages of clinical testing.

In concert with basic science efforts to develop new vaccines and microbicides[5] there is need for studies to determine the most optimal cohorts for their evaluation. As these interventions are developed there is need to identify cohorts[6] in which their efficacy can be tested. Conduct of HIV-1 vaccine and microbicide trials requires cohorts that have sufficiently high incidence of HIV-1 infection. The high antenatal HIV-1 seroprevalence rates of (10-30)% in many urban centers in Kenya suggest a high underlying incidence of the HIV/AIDs. Thus in Kenya, women participating in perinatal HIV prevention trials may be suitable for vaccine and microbicide trials due to the useful infrastructure and a follow-up schedule for the women in these Anti-Natal Clinics (ANC).

In high prevalence areas such as Sub-Saharan Africa, WHO recommends that HIV-1 vaccination programs will need to include a wider segment of the population. This will help the researchers determine the factors which are likely to explain the willingness to participate HIV/AIDs vaccine trials. Using participants in perinatal HIV-1 prevention trials for vaccine and microbicide studies possess several advantages. First, these provides an adquate infrastructure and easy follow-up visits as the mothers come for the post-natal clinic after delivery. These are not applicable with the other general populations. The loss to follow-up in such cases could pose serious challenges.

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[2]occurs when new cases of a certain disease occur in a given human population, during a given period, substantially exceeding the expected recent experience.

[3]HIV subtype

[4]a biological substance that improves immunity.

[5]compound/substance whose purpose is to reduce the infectivity of microbes, such as virus or bacteria.

[6]same characteristic grouping of items.

Secondly, compared to high-risk groups, women participating in Prevention of Mother-To-Child Transmission (PMTCT) programs are more representative of reproductive birth giving cohort. Compared to women in stable relationships, women in high risk groups are more likely to have multiple partners, sexually transmitted diseases, genital tract injuries and exposure to diverse viral subtypes which may affect the efficacy[7] of vaccines and microbicides.

Third, unlike commercial sex workers, many women in stable relationships are at risk of HIV-1 infection, not from their own behavior but that of their sexual partners whose behavior may change dramatically with study participation. Thus study participation may not be associated with a dramatic reduction in HIV-1 infection risk among women in stable relationships like has been shown in previous studies among commercial sex workers participating in prospective HIV-1 incidence studies.

1.2 Problem Statement

Most studies have found consistently high levels of knowledge regarding vaccines generally, and potential HIV-1 vaccines in particular. However, there has been limited efforts in modelling the willingness to participate in HIV vaccine trials. Limited statistical work has been caried out on the data arising from such surveys. Previous studies have concentrated on the descriptive aspects of the factors influencing willingness of study participants in HIV/AIDS vaccine trials.

Thus, the current study entails finding a suitable model which relates willingnes to the factors influencing it. The model of the ordered responses on willingness to participate is utilized in predicting this sub-set of participants likely to be involved and subsequent uptake of the vaccine/microbicides.

[7] capacity to produce effect.

1.3 Study Objectives

1.3.1 General Objective

The general aim of the study was to use ordered logistic regression to determine a parsimonious model which explains willingness of women in perinatal prevention programs to participate in a vaccine/microbicide trials.

1.3.2 Specific Objectives

1. Develop a suitable ordered logistic regression model for willingness of perinatal women to participate in a vaccine/microbicide trials, and
2. Determine factors associated with the willingness to partipate in a vaccine/micribicide trials.

1.4 Significance of the Study

Although HIV/AIDS prevalence in Kenya has shown a steady decline, it is still a major challenge to our socio-economic development. Further insight is needed to strengthen the national response. This can be achieved through a well-coordinated national research agendas and statistical informed decision making. HIV and AIDS continues to ravage every sector of Kenyas economy. The pandemic has left behind millions of orphans and created widespread poverty and helplessness among the population. Today, HIV and AIDS is recognized as a threat to human development and thus requires concerted efforts from all stakeholders in order to reverse the trend.

In the absence of a cure for HIV and AIDS, designing preventive measures to stem the pandemic[8] still remain to be the best options. Vaccination is undoubtebly one of such measures.

[8]disease that spreads over a whole country/the whole world.

For instance, vaccination proved successfull in steming small pox and has had tremendous impact in the control of polio. Similarly, vaccination is key in the control of HIV and AIDS.

Thus, understanding the ultimate cohort of individuals willing to participate in the vaccine trials will be of great material to researchers as to the best factor combinations to consider in search for HIV and AIDS vaccine and reduce cost due to loss-to-follow-up such studies.

Chapter 2

Literature Review

Previous studies have been done on the acceptability to participate in HIV/AIDS vaccine though by medical doctors in different regions of the world. A growing body of literature has investigated willingness to participate in preventive HIV-1 vaccine trials. Besides providing estimates of interest, assessing willingness may identify conditions which foster or inhibit the motivation to join trials, as well as identify important population differences. Most studies have found consistently high levels of knowledge regarding vaccines generally, and potential HIV-1 vaccines in particular. Differences in willingness to participate in the vaccine trials dependent mostly on the levels of knowledge and due to cultural and group specific attitudes towards the vaccines.

For instance, in Uganda a study by Hom D. L. et al (1993), a total of 570 volunteers aged between 19 and 22 years old were screened for HIV-1, with a resulting seroprevalence rate of 18.3%. Of the total volunteers a cohort of 249 HIV-1 non-infected military recruits in the Ugandan Peoples Defense Forces (UPDF) was followed prospectively[1] for 18 months to document rates of HIV-1 seroprevalence, seroconversion, and knowledge and attitudes related to vaccine acceptability. At the 3 and 12 month visits, participants were interviewed on issues of acceptance and knowledge about vaccines, including anti-HIV vaccines in particular. More than 90 per cent believed that HIV vaccines will not cause HIV infection, and if offered, 88% reported that they would take the vaccine if they were not already infected. Non-vaccine prevention methods were considered less reliable; monogamy and condom use were considered effective by 33.5% and

[1] follow-up studies where participants have a starting point and then follow-up is done for some time until an event is obseved.

69.3% of the cohort respectively. After completing the vaccine acceptability questionnaire at the 12 month visit, subjects were offered an approved polyvalent meningococcal vaccine as an indicator of general vaccine acceptance. All subjects reported receiving at least one previous vaccination, and 95% willingly accepted the meningococcal vaccination.

In India, Sahay S. et al (2004) in a study on willingness to participate in HIV vaccine trials among low and high risk populations found that the overall willingness to volunteer for HIV vaccine trials was 48%. Factors associated with increased willingness to participate in these trials were awareness of current HIV vaccine efforts (Odds Ratio (OR)=2.4, p-value$= 0.002$), insurance as incentive (OR $= 2.4$, p-value $= 0.009$, altruism (OR $= 4.7$, p-value< 0.001) and lack of concern about post-trial refusal of sex by partners (OR $= 2.3$, p-value $= 0.011$)

Van de Ven P. et al (2005) conducted a study in Australia on the willingness to participate in HIV vaccine trials among HIV-negative gay men. This study aimed at determining and describing HIV-negative gay men's willingness to participate in HIV vaccine trials. Data were from participants who completed face-to-face interviews during the first 18 months of recruitment into the Health in men cohort of HIV-negative gay men. A key outcome measure was a scale of willingness to participate in HIV vaccine trial, with scores ranging from 1 (unwilling) to 4 (willing). Nine hundred and three (903) participants aged between 18 and 75 years with the median age of 36 years. Mean of Willingness to Participate in HIV vaccine trials was 2.53 (standard deviation $= 0.5$), with approximately 51% of the men scoring greater than the mid-point of 2.5 score.

In this study a reduced linear regression model[2] yielded four significant independent associations with willingness to participate in HIV vaccine trials namely lack of tertiary education (p-value < 0.001), having engaged in sex for the previous six months in any unprotected intercourse with casual or non-concordant regular partners (p-value < 0.001), higher self-rated likelihood of HIV infection (p-value < 0.001), and higher mean scores on a scale of comfort with participation in HIV vaccine trials (p-value< 0.001). The willingness of HIV-negative gay men at potentially higher risk for HIV to participate in HIV vaccine trials augurs well for enrolment in HIV vaccine efficacy trials.

Buchbinder S.P. et al (2004) in San Fransisco, United States of America (USA) studied the determining determinants of enrollment in a preventive HIV vaccine trial, hypothetical versus actual willingness and barriers to participation. In this study, participants previously enrolled in

[2]model with less factors compared to the full model.

an HIV Vaccine Preparedness Study (VPS) in 8 USA cities were invited to be screened for a phase II [3] HIV vaccine trial. Demographic and risk characteristics of those enrolling, ineligible, and refusing enrollment were compared. In this study a multi-nomial[4] logistic models were used to identify independent predictors of refusal and the willing to participate.

Of 2,531 high-risk HIV-uninfected participants contacted for the vaccine trial, 13% enrolled, 34% were ineligible, and 53% declined the enrollment. Only 20% of those stating hypothetical willingness during the VPS actually enrolled in for vaccine trial. In multivariate analysis, refusal was higher among African Americans and lower in persons > 40 years of age, those attending college, and those with ≤ 5 partners in the prior 6 months. All racial ethnic groups cited concerns about vaccine-induced seropositivity; African Americans also cited mistrust of government and safety concerns as barriers to enrollment.

De Souza C.T. et al (2003) carried out a study on willingness to participate in HIV vaccine trials among a sample of men who had sex with men, with and without a history of commercial sex in Rio de Janeiro, Brazil in 2003. The study objective was to assess willingness of men who have sex with men (MSM) enrolled in a vaccine preparedness study to participate in phase III[5] anti-HIV/AIDS vaccine trials. Overall, 57% of participants stated they would participate in a putative vaccine trial. MSM who reported commercial sex work were significantly (p-value < 0.05) more likely to engage in risky behaviours than others. In bivariate analysis, commercial sex workers (CSWs) were significantly (p-value < 0.05) more likely than non-commercial sex workers (NCSWs) to be willing to participate in vaccine trials 62.6% versus 51.4%. Among those willing, CSWs reported significantly more often (p-value < 0.05) (50.5%) than NCSWs (38%) that they would enroll to protect themselves from HIV.

On running the multivariate analyses, variables associated with Willingness To Tarticipate (WTP) were lower educational level, positive serology for syphilis, and engagement, under the influence of alcohol, in risky sexual practices that would normally be avoided, but not commercial sex work. The potential enrollment in vaccine trials of MSM CWSs, as well as participants of low socio-economic status and high risk.

[3] initial clinical investigation for treatment effects. concerned with safety and efficacy for patients.($n = 50$ to 100)

[4] more than 2-variables

[5] full-scale evaluation of treatment comparison of drug versus control/standard in (large) trials (n=100 to 1,000)

Meyers K. et al (2001) in their study on HIV vaccine trials, on intravenous drug users were 52% of the subjects, expressed willingness to be one of the first individuals to participate in a preventive HIV vaccine efficacy trial. Subjects who had recently shared needles or works and subjects who trusted the government to ensure vaccine safety were both twice as likely to report interest in participation. Twenty-two percent of subjects reported that they would increase needle sharing if vaccinated. 30 per cent did not know what a vaccine was. These findings suggest that some in-treatment intravenous drug users would volunteer for a preventive HIV vaccine efficacy trial. Education and counseling will be required to ensure that subjects fully understand the trial's purposes, methods, risks and benefits.

Acceptability and willingness to participate in vaccine trials is often assessed through cross-sectional surveys, and expression of willingness to participate may not translate into participation or continued follow-up. Evaluation of baseline willingness to participate combined with a prospective 1 year follow-up may get closer to the truth regarding actual willingness to participate and follow-up in a vaccine or microbicide trial.

Smit J. et al (2006) in a study on willingness to participate in HIV vaccine research in a peri-urban South African community interviewed 198 individuals in a peri-urban South African community immediately after enrolment into an HIV vaccine preparedness study on their willingness to participate in hypothetical vaccine trials. Overall 23% of participants said that they would be willing to participate in an HIV vaccine trial. Willingness was associated with increasing age, male gender, and increasing knowledge about vaccines generally and HIV vaccines specifically. On multivariate analysis, a 1-unit increase in HIV vaccine knowledge score was associated with a 10-fold increase in willingness to participate (OR = 10.72, 95% CI = 4.40 to 26.12).

Chapter 3

Methodology

3.1 Data

3.1.1 Survey

The survey was conducted on women attending perinatal prevention prgrams at Mathare Anti-Natal Clinic. A prospective observational cohort study of HIV-1 seronegative women identified during pregnancy.

At enrollement 808 participants were interviewed, in which the knowledge, attitude and willingness to participate in the study was assessed. On the willingnsess to participate in the study only 11 (1.0%) participants were undecided on whether to participate in the study or not. Thus, a total of 797 cases were analysed for definitely willing, somewhat willing and not willing. In the prospective follow-up, 74, 55, 49 and 9 participants came back at Month 3, Month 6, Month 9 and 1 year respectively. In the last visit (1 year), only 9 participants came for evaluation with all willing to participate in the vaccine trials, these cases were omitted from the analysis and analysis carried out upto month 9 of the follow-up.

3.1.2 Data Management

The data was collected using structured questionnaires. After cross-checking for errors the data was entered in Access Data Base. Data was later exported to Statistical Package for Social Scientists (SPSS) version 13.0 for further cleaning and management and later to R-2.9.0 for analysis. On some cases analysis was also done using STATA version 10.0.

3.2 Regression Model

3.2.1 Introduction

Regression is one of the most widely used statistical techniques for analyzing observational data. Regression models are used to uncover net relationships between an outcome, or response variables and a few explanatory variables while controlling for confounding factors. Regression models are used to meet different research goals. Sometimes, regression modelling is aimed at learning the causal effects of one variable, or a set of variables, on a dependent variable. Other times, regression models are used to predict the value of a response variable. Regression models are also often intended as short-hand summaries providing a description linking a dependent variable and independent variable.

Like most methods (mean, median e.t.c) in statistics, regression is also used as data-reduction technique from a large amount of raw data to summary statistics. It presents essential information without much distortations, like any other procedure including tables or group specific means and variables.

In regression analysis, the objective is to predict as closely as possible, an array of observed values of the dependent variable based on a simple function of independent variables. Obviously, predicted values from regression models are not the same as observed data points. Characteristically, regression partitions an observation into two parts:-

$$Observed = Structural + Stochastic.$$

The observed part represents the actual values of the dependent variable at hand. The structural part denotes the relationship between the dependent and independent variables. The stochastic part is the random component unexplained by the structural part. In general, the last term may be regarded as the sum of three components, namely, "omitted structural factors", "measurement error", and "noise".

The type of regression to apply is depicted by the type of data at hand, that is, the data response variable can assume a quantitative/numerical or it can assume a qualitative/categorical case as summarised in the table below;

Table 3.1: **Typology of Regression Models**

Dependent Variable	Independent Variable	Method of Analysis
Continuous	Continuous	Regression, Correlation
Continuous	Categorical	Regression, ANOVA
Binary	Categorical	Logit/Probit/Loglinear
Binary Unordered Polytomous	Continuous	Logit/Probit
Binary Unordered Polytomous	Categorical	Loglinear/Multinomial Logit
Unordered Polytomous	Continuous	Multinomial Logit
Ordered Polytomous[1]	Categorical	Ordered Logit/Probit/Loglinear
Ordered Polytomous	Continuous	Ordered Logit/Probit
Cross-classified Data	Categorical	Loglinear
Censored Duration Data	Continous/Categorical	Loglinear/Logit/Comp.Log-Log

Source:- Statistical Methods for Categorical data analysis by Daniel A. Power.

[1] This is the model employed in the current study

The first 2 cases represents the classical approach for conditional mean estimation, while 3 and 4 involves binary response variables and 5 to 8 are the ordered and the unordered response variable. Since the outcome variable of the study is an ordered polytomous independent variables the appropriate method of analysis will be ordered logit model.

3.2.2 Scoring Methods for Ordinal Dependent Variables

Ordered categorical variables assume numerical values to denote rank-order of a particular attribute. These rankings, however, do not neccesarily represent the actual magnitudes on a substantive scale. Usually, the ordinal variables could be viewed as somewhere in between nominal variables and on the other hand as continous. Ordinal variables are more general than continuous variables in allowing for varying distances across adjacent values but more restricted than norminal variables in containing ordinal information. Examples of ordinal qualitative data include the likert scale, in which responses on questions take such categories as, definitely willing, somewhat willing and not willing.

Incomplete information is one of the fundemental problems facing the analysis of ordered dependent variables. An ordinal variable reveals the rank order of its different values but not their magnitudes on a substantively meaniful scale. To address this, various ways to recover the information partaining the magnitudes by assigning numerical score to the categories, a method now popularily known as the "**Scoring Method**".

The simplest and perhaps most popular method of scoring is the integer scoring. This method assigns integers to represent the rank order for example, a typical likert-scaled, one may assign, definitely willing = 1, some what willing=2, and not willing=3. The crucial assumption underlying integer scoring is that the distance between adjacent category are all equal. This will be applied in the study. Another type of scoring is called the mid-point. Sometimes ordinal variables results from categorical measures that are conceptually continous, for example, the age of the patients. Later the research might be interested in the grouped categories of the age resulting to mid-point scoring. This scoring method poses two potential problems; (i) if the data distribution is highly skewed within an interval, mid-points are poor estimates, and (ii) incases where the last interval is open ended the mid-points usually poses a misleading information.

3.2.3 Logit Models for Grouped Data

Regression models for a dichotomous dependent variable y, we define the logit function as

$$\log\left(\frac{p}{1-p}\right) = \log\left[\frac{P_r(Y=1)}{P_r(Y=0)}\right] \tag{3.1}$$

that is, as logged ratio of two probabilities.

In general for an outcome variable y with multiple responses ($j = 1, \ldots, J$), the logit transformation takes the form,

$$\log\left[\frac{P_r(Y=j)}{P_r(Y=j')}\right] = \log\left(\frac{p_j}{p_{j'}}\right) \tag{3.2}$$

where p_j and $p_{j'}$ are respectively, probabilities for categories j and j'.

In addition, logits can be conducted using cumulative probabilities. Thus, many potentially interesting logits exists for a response variable with multiple outcome. Of the many logits for a j^{th} category response variable y ($j = 1, \ldots, J$), however, only $J - 1$ logit are non-reduntant.

Withuot loss of generality, we contrast all other responses to the baseline category, which in most cases is the first category. The baseline logit for the j^{th} category ($j = 2, \ldots, J$) is defined as

$$\begin{aligned} BL_j &= \log\left[\frac{P_r(Y=j)}{P_r(Y=1)}\right] \\ &= \log\left(\frac{p_j}{p_1}\right) \qquad\qquad j = 2, \ldots, J \end{aligned} \tag{3.3}$$

The choice of the first category as the baseline is entirely arbitrary, with the basic idea to cantrast a pair of adjacent categories.

The adjacent logit for the j^{th} category is defined as

$$\begin{aligned} AL_j &= \log\left[\frac{P_r(Y=j)}{P_r(Y=j-1)}\right] \\ &= \log\left(\frac{p_j}{p_{j-1}}\right) \qquad\qquad j = 2, \ldots, J \end{aligned} \tag{3.4}$$

We can use the cumulative probabilities to define the cumulative logit as

$$\begin{aligned} CL_j &= \log\left[\frac{P_r(Y\leq j)}{P_r(Y>j)}\right] \\ &= \log\left(\frac{\sum_{k=1}^{j} p_k}{\sum_{k=j+1}^{J} p_k}\right) \end{aligned} \tag{3.5}$$

to be the cumulative logit that the probability is less than or equal to j versus greater than j.

From the equations (3.3) and (3.4), it is clear that,

$$BL_j = \sum_{k=2}^{j} AL_k \tag{3.6}$$

Assuming one categorical independent variable $\underline{x}$ the adjacent category logit model takes the form

$$\begin{aligned} \log\left(\frac{p_j}{p_{j-1}}\right) &= \beta_{uj} \\ &= \text{A Saturated Model}^2 \qquad u = 1, \ldots, U, \quad j = 2, \ldots, J \end{aligned} \tag{3.7}$$

where; $(u = 1, \ldots, U)$, are factor levels of the categorical variable.

If we assume that the explanatory variable is an interval-level variable, equation (3.7) can be simplified as

$$\log\left(\frac{p_j}{p_{j-1}}\right) = \alpha_j + \underline{\beta}_u \underline{x}'_u, \quad u = 1, \ldots, U, \quad j = 2, \ldots, J \tag{3.8}$$

where $\underline{\beta}_u$ is a vector of regression coefficient corresponding to the levels of the factor in consideration.

The intercepts are $J-1$ and the regression coefficients associated with the levels of the factor in consideration are $(J-1)U$, thus, the total number of parameters is

$$J - 1 + (J-1)U = (J-1)(U+1) \tag{3.9}$$

In general, for V categorical independent variables the number of parameters is

$$(J-1)(U_1 + U_2 + \cdots + U_v + 1) \tag{3.10}$$

where; $(U_1, U_2, \ldots, U_v$, are factor are the number of levels for the factors respectively.

[2]The model with all the factors

3.2.4 Ordered Logit and Probit Models

These models are commonly referred to as ordered (or ordinal) logit and probit model. There exists two approaches to extending the binary logit and probit model to the case of ordered outcomes namely,

1. The use of the logit or probit of cumulative probabilities - This approach is normally prefered when the categories are ordered but the analyst is unwilling to assume that the outcome represents are ordered or collapsed version of a continous variable that would possibly be measured more finely, and
2. The second approach assumes the existence of an underlying continous latent variable, a kin to random-utility regression type models for binary response presented.

Regardless of which approach is used, the statistical properties of the models are similar.

Given that the response variable y_i assumes the values $1, 2, \ldots, J$, $(J \geq 3)$ which corresponds to ordered responses, a general probability model can be written in terms of cummulative probabilities. The cumulative probability for the i^{th} individual upto response level j, denoted as $C_{i,j}$, can be written as

$$C_{i,j} = P_r\left(Y_i \leq j\right) = \sum_{k=1}^{j} P_r\left(Y_i = k\right), \qquad i = 1, \ldots, n, \;\; j = 2, \ldots, J \tag{3.11}$$

By definition the cumulative probabilities are equal to one when $j = J$, meaning that $C_{i,j} = 1.0$ for all $(i, j)'s$.

We now let the cumulative probability be a function of a vector of independent variables, $x_{i's}$ as

$$C_{i,j} = F\left(\alpha_j + \underline{x}'_i \underline{\beta}_i\right), \qquad i = 1, \ldots, n, \;\; j = 2, \ldots, J \tag{3.12}$$

where $F(.)$ follows a cumulative logistic distribution. The ordered logit model is obtained when $F(.)$ follows a cumulative distribution. Choosing a cumulative standard normal distribution for $F(.)$ leads to the ordered probit model.

In this specification, the parameters α_j are $J-1$, which can be thought of as cutpoints thresholds, or separate intercept, corresponding to the ordered categories of the dependent variable. Defining the cumulative probabilities in this way means that;

$$C_{i,j} > C_{i,j-1} \tag{3.13}$$

so that $F(.)$ increases with j.

Thus the $C_{i,j}$ parameters are necessarily non-decreasing in j.

The conditional probabilities of the ordered outcomes can be written in terms of the cumulative probabilities as

$$\Pr(Y_i = j|\mathbf{x}_i) = \begin{cases} F(\delta_1 - \underline{x}'_i\underline{\beta}_j) & j = 1 \\ F(\delta_j - \underline{x}'_i\underline{\beta}_j) - F(\delta_{j-1} - \underline{x}'_i\underline{\beta}_j) & 1 < j \leq J-1 \\ 1 - F(\delta_{J-1} - \underline{x}'_i\underline{\beta}_j) & j = J \end{cases} \tag{3.14}$$

where $\delta_{j's}$ are cutpoints for the latent variable approach similar to $\alpha_{j's}$ for the cummulative probability approach in that they function to fit exactly the marginal distribution of outcome category.

In this way the predicted probabilities associated with a response can be retrived from the model.

The ordered logit model is obtained by specifying the cummulative probabilities

$$\begin{aligned} C_{i,j} &= \Pr(Y_i \leq j|x_i) \\ &= \frac{\exp(\alpha_j + \beta x_i)}{1 + \exp(\alpha_j + \beta x_i)} \end{aligned} \tag{3.15}$$

This model is linear in the logistic scale.

Letting $L_j(x_i)$ denote the cummulative logit of $y_i \leq j$ versus $y_j > j$, we have

$$L_j(x_i) = \log\left[\frac{\Pr(Y_i \leq j/x_i)}{\Pr(Y_i < j/x_i)}\right] \tag{3.16}$$

This model is often called the proportional ODDS model. Given two covariate vectors, x_1 and x_2, the odds of a response $y_i \leq j$ versus $y_j > j$ are proportionally higher or lower across the two situations $x_i = x_1$ and $x_i = x_2$.

Letting $w(x_h), (h = 1, 2)$, denote the cummulative odds associated with covariate values, one obtains the cummulative odd ratio as,

$$\begin{aligned}\frac{w(x_1)}{w(x_2)} &= \frac{\Pr(Y_i \leq j|x_1) / \Pr(Y_i > j|x_1)}{\Pr(Y_i \leq j|x_2) / \Pr(Y_i > j|x_2)} \\ &= \frac{\exp(\beta x_1)}{\exp(\beta x_2)} \\ &= \exp\Big(\beta(x_1 - x_2)\Big) \end{aligned} \tag{3.17}$$

Which is proportional to the distance between the values of the explanatory variables. The log of the cummulative odds-ratio, or cummulative log-odds-ratio is;-

$$\begin{aligned}\log\left[\tfrac{w(x_1)}{w(x_2)}\right] &= L_j(x_1) - L_j(x_2) \\ &= \beta(x_1 - x_2) \end{aligned} \tag{3.18}$$

For J ordered categories and single covariate the fitted logits correspond to $J - 1$ parallel lines. It is also possible to test for equal slopes. When $\beta_k > 0$, the cummulative logits increases. This means that y tends to be smaller for higher values of x_k. Similarly, when β_k is negative, increases in x_k are associated with higher levels of y.

The ordered probit model can be obtained by specifying the following conditional cummulative probabilities

$$\begin{aligned} C_{i,j} &= \Pr(Y_i \leq j|x_i) \\ &= \Phi(\alpha_j + \beta x_i) \end{aligned} \tag{3.19}$$

where $\Phi(.)$ denotes the cummulative standard normal distribution function. The ordered logit and probit are special cases of cummulative link models.

3.2.5 Estimation and Hypothesis Testing

(i) Estimation

The goal of this is to find estimates of β_{uj} $(u = 1, \ldots, U)$ and α_j $(j = 1, \ldots, J-1)$ in equation (3.8), that maximize the joint probability of the observed value. The contribution to the likelihood for the i^{th} observation depends on which value of j is observed. For each of the J values of the ordered response, we take the product over all observations for which $y = j$ and hence the likelihood function is,

$$L = \prod_{i=1}^{n} \prod_{j=1}^{J} \Pr(Y_i = j|x_i)^{\delta_{ij}} \tag{3.20}$$

where $\delta_{ij} = 1$ if $y_i = j$ and 0 otherwise, and n is the sample size.

(ii) Hypothesis Testing

The hypothesis of interest is

H_0 : There is no significant association between the willingness to participate in a vaccine/microbicide study and baseline factors;

Versus

H_1 : There is significant association between the willingness to participate in a vaccine/microbicide study and baseline factors

For Categorical variable we have

H_o : $p_{uj} = p_{u.}p_{.j}$ for $u = 1, 2, \ldots, U$ and $j = 1, 2, \ldots, J$,

versus

H_1 : The hypothesis H_o is not true.

Test statistic for composite **NULL** hypothesis is,

$$\begin{aligned} Q &= \sum_{u=1}^{U}\sum_{j=1}^{J}\frac{(N_{uj}-\hat{E}_{uj})^2}{\hat{E}_{uj}} \\ &\sim \chi^2_{(U-1)(J-1)}, \quad as \quad n\to\infty \\ &\sim \chi^2_{(UJ-U-J+1)} \quad \text{for each factor under consderation.} \end{aligned} \tag{3.21}$$

where, N_{uj} and E_{uj} are the observed and expected frequencies respectively.

In this case U = the Rows (The factor levels for the factor in consideration), and J = Column (The ordered response, in this case J=3, definitely willing, somewhat willing and not willing.)

For such cases, the $Q_{computed}$ is compared with the Q_{table}, and reject H_0 at α - level of significance if $Q_{comp.} > Q_{tab}$.

3.3 Data Analysis and Model Adequacy

3.3.1 Data Analysis

In an ordered logistic regression model, the parameter estimates can be compared to a baseline category (Rank). In this scenario, definitely willing to participate was used as the baseline category.

The data was analysed using R.2.9.0 and STATA version 10.0 while the management of the same was by both MS Access and SPSS respectivey.

3.3.2 Model Adequacy

(i) Generalized Likelihood Ratio Statistic

The likelihood functions for the maximal model and the model of interest can be evaluated at the respective maximum likelihood estimates $(\underline{\hat{\alpha}}, \underline{\hat{\beta}})_{max}$ and $(\underline{\hat{\alpha}}, \underline{\hat{\beta}})$ to obtain values $L((\underline{\hat{\alpha}}, \underline{\hat{\beta}})_{max}; \underline{\mathbf{y}})$ and $L((\underline{\hat{\alpha}}, \underline{\hat{\beta}}); \underline{\mathbf{y}})$ respectively.

$$\lambda = \frac{L((\underline{\hat{\alpha}}, \underline{\hat{\beta}})_{max}; \underline{\mathbf{y}})}{L((\underline{\hat{\alpha}}, \underline{\hat{\beta}}); \underline{\mathbf{y}})} \tag{3.22}$$

is a measures of goodness of fit. The log of equation (3.22) is

$$\begin{aligned} \log\lambda &= \log L((\underline{\hat{\alpha}}, \underline{\hat{\beta}})_{max}; \underline{\mathbf{y}}) - \log L((\underline{\hat{\alpha}}, \underline{\hat{\beta}}); \underline{\mathbf{y}})) \\ &= l((\underline{\hat{\alpha}}, \underline{\hat{\beta}})_{max}; \underline{\mathbf{y}}) - l((\underline{\hat{\alpha}}, \underline{\hat{\beta}}); \underline{\mathbf{y}})) \end{aligned} \tag{3.23}$$

Large values of $\log\lambda$ suggest that the model of interest provides a poor description of the data.

(ii) Log-Likelihood Ratio Statistic (Deviance) as

We define the log-likelihood ratio statistic

$$D = 2\log\lambda \tag{3.24}$$

If the model is correct,

$$D \sim \chi^2_{n-p,\alpha} \tag{3.25}$$

where p is the number of parameters in the model, Reject the model if $D > \chi^2_{n-p,\alpha}$ at α-level of significance.

Chapter 4

Application of the Model

4.1 Choice of Variables

The dependent variable is classified into three ordered categories as shown in table (4.1) below.

4.1.1 Dependent variable (Outcome)

Table 4.1: **Dependent (Outcome) Variable Classification**

Category	Descriptions
1	Definitely Willing to Participate in a Vaccine/Microbicide Trial
2	Somewhat Willing to Participate in a Vaccine/Microbicide Trial
3	Not Willing to Participate in a Vaccine/Microbicide Trial

Study participants were asked on their willingness to take part in a study that required them to receive a vaccine/microbicide to test if it protects them against HIV.

4.1.2 Independent variables(Predictors)

Independent variables are classified into various categories as shown in table (4.2).

Table 4.2: **Independent Variable Classification**

Independent Variable	Descriptions/Categories
Socio-demographic	Age,Eduaction levels,Marital Status,Employment and Number of rooms,Occupants,Monthly rent
Knowledge of Vaccine and Microbicides	HIV Transmission,Heard of Vaccine,Heard of Vaccine against HIV and ever Heard of Microbicides to prevent HIV Transmission
Attitude	Effectiveness of the current Vaccines
Past Sexual History	Parity, Age at Menache, Sexual Partners,History of STDs, Duration with current partner, Partners monogomus, Few risk of HIV

The explanatory variables included, the socio-demographic factors, knowledge on the prevention of HIV/AIDS, whether they had ever heard of a vaccine in general and also whether they had ever heard of a vaccine against HIV?

Attitude to vaccines and microbicides was also accessed, whereby knowledge of the existing vaccines, their effectiveness and side-effects was sort. Participants were expected to rank in ranges of percentages on how they thought the current available vaccines prevented diseases and their associated side-effects. The expectations on how effective the future HIV vaccine will be and its expected side-effects was also sort. These factors were suspected to be limitation to willingness of the participants in the uptake of the vaccine.

The past sexual history and the obstetric history of the participants was of key interest and in this section parity, age at menarche, number of sexual partners, ever had an STD and duration of stay with the current partner was evaluated.

4.2 Descriptive Aspects

At enrollment study participants were assessed for the willingness to participate in the study and this was repeated after every 3 months upto 1 year. At enrolment a total of 797 participants took part. Prospectively, 74, 55, 49 and 9 at month three, six, nine and at one year. Due to the limited cases at year 1 the data was analysed upto month 9. The descriptive aspects at enrollment are included in table 4.3 below.

Table 4.3: **Socio-Demographic Factors (Continuous Variables)**

Factor	Mean (SE)	Median	Range (Min. to Max.)
Age (in Years)	24.0(0.2)	23.0	17-41
Years of School	8.7(0.1)	8.0	0-16
No.of rooms	1.2(0.0)	1.0	1-5
No.of Pple	3.3(0.1)	3.0	1-13
Monthly rent	1,641.3(33.9)	1,600	200-7,000

The age of the participants ranged between 17 and 41 years of age. The mean age was 24 years with the median age being 23 years. The interquartile range for the participants was 6 years (20 to 26), indicating that the participants were in their early twenties as shown in figure 4.1 below.

Most participants had been to school for an average of 9 years translating to most of them having acquired basic primary education. Average number of the rooms among the participants was one room, though it ranged between 1 and 5 with the average monthly rent was KSH. 1,600 with the average people per room being 3.3 and it ranged between 1 and 5 people.

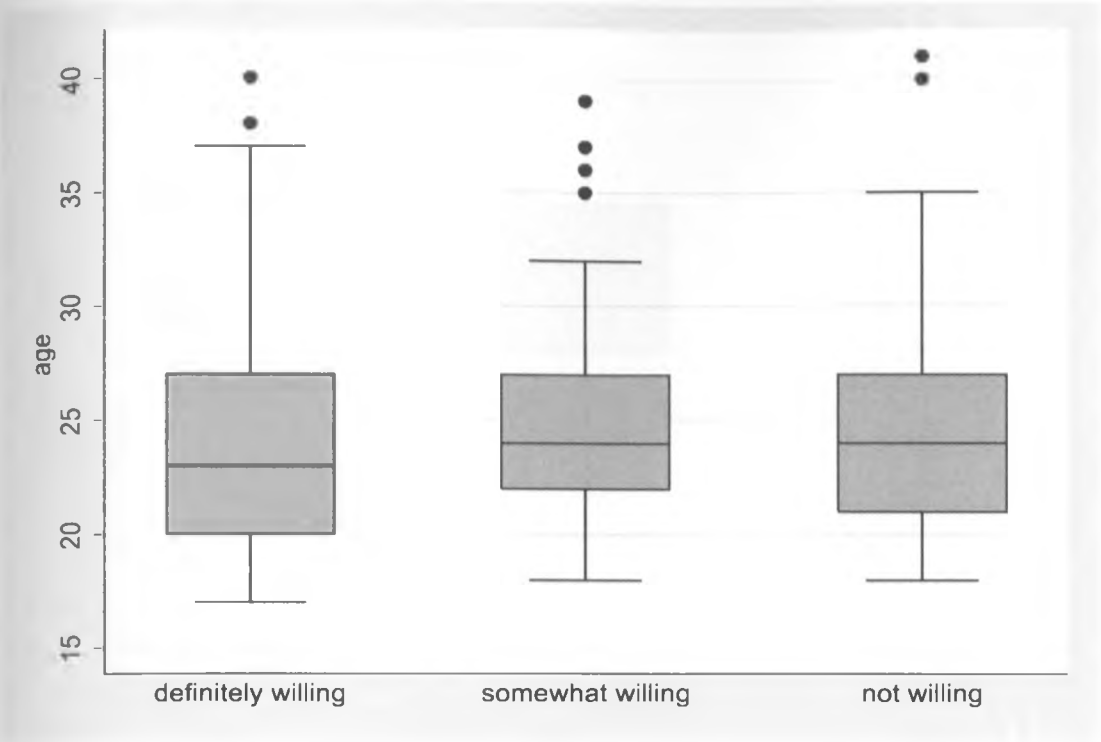

Figure 4.1: Box plot of age distribution in years

From the figure above, it can be deduced that the mean age over the different categories of willingness is almost the similar.

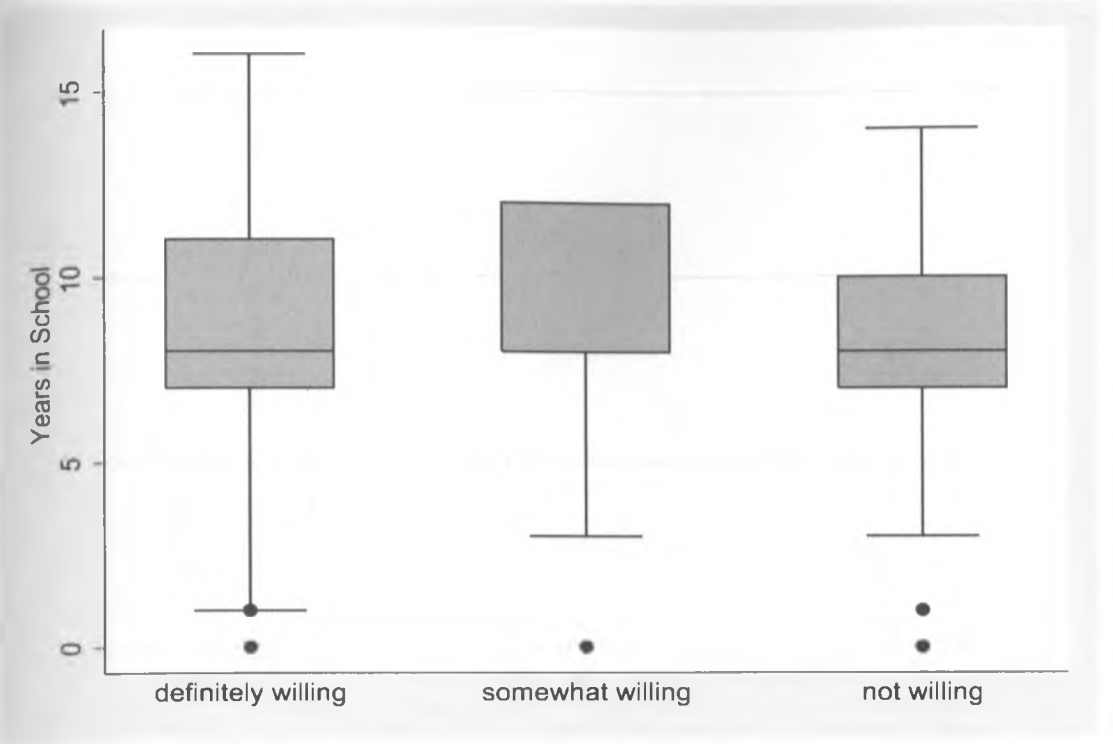

Figure 4.2: Box plot of school age

The mean age over the different categories of willingness is not significantly different.

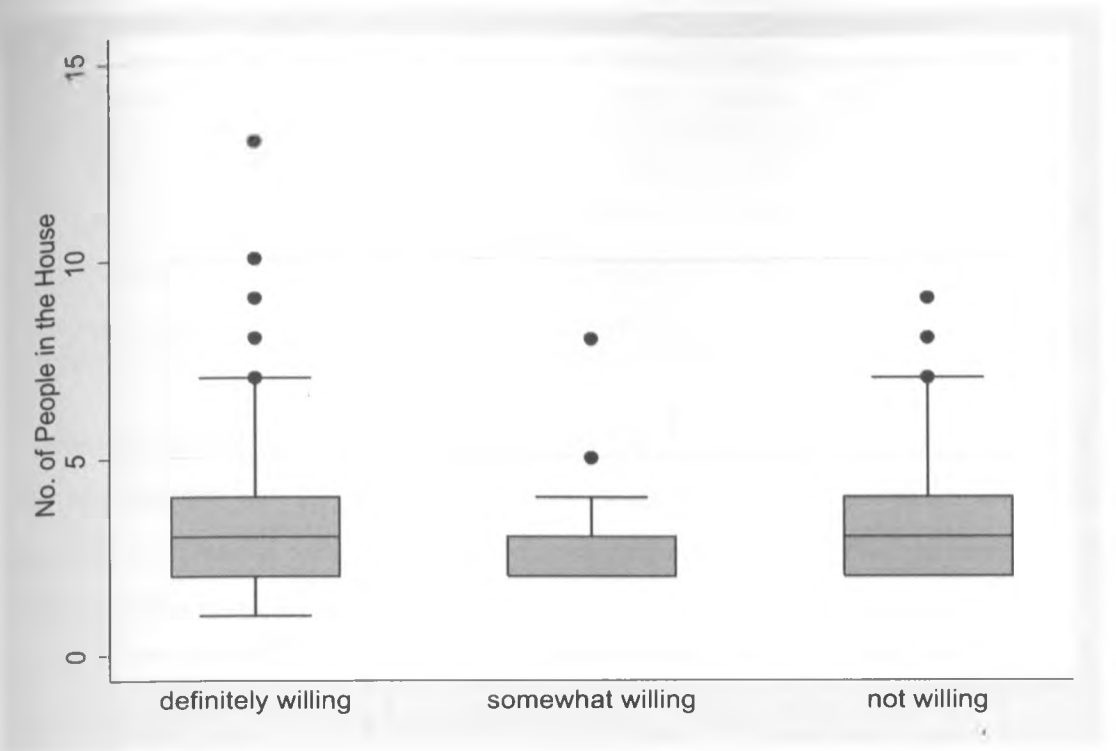

Figure 4.3: Box plot of number of people living in the house

The mean number of people in the house for those definitely willing to participate was 3.2, somewhat willing was 3.2 and those not willing was 3.5. However, the mean number of people is not different across the categories of willingness.

Table 4.4: **Sexual History**

Factor	Mean (SE)	Median	Range (Min. to Max.)
Parity	2.2(0.0)	2.0	0-8
Age at Menarche	17.4(0.1)	17.0	9-28
No. of sexual partners	2.5(0.1)	2.0	1-40
How long with current partner	4.2(0.1)	3.0	1-25

Average number of children per participant was 2 children, with a range of 0 to 8 children. Age at manarche was 17 years, although the range was between 9 and 28 years. On average the number of sexual partners was 3 and it ranged between 1 and 40 partners indicating risky behaviours the participants were exposed to.

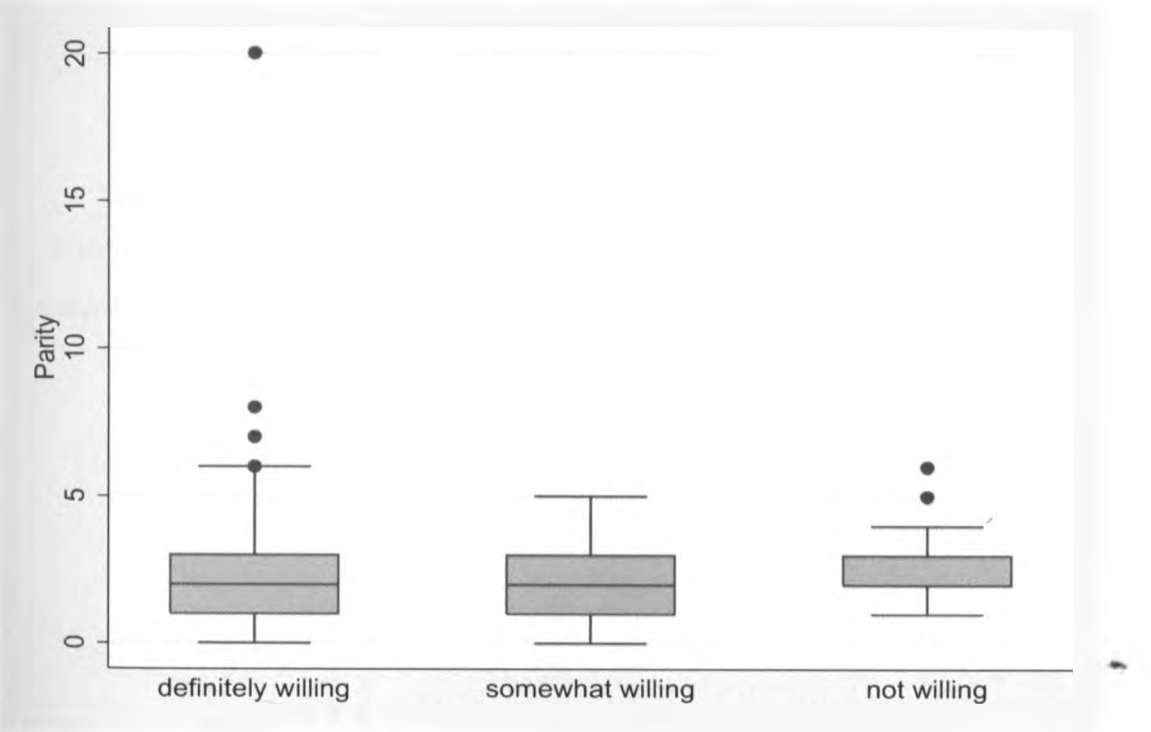

Figure 4.4: Box plot of parity

Participants definitely willing to particpate in the vaccine trial had an average of 2 children as compared to 2.4 for those not willing and somewhat willing.

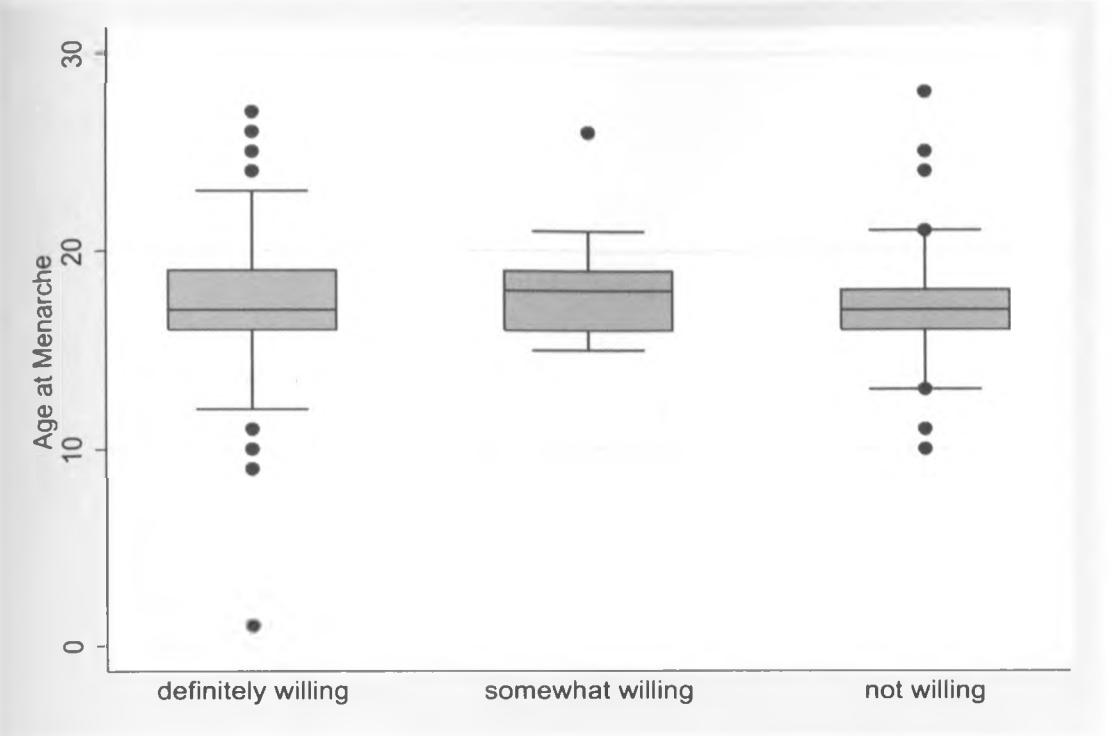

Figure 4.5: Box plot of age at menarche

Participants in the study had their first sexual encounter at an average of 17 years, this was the same across the willingness to participate.

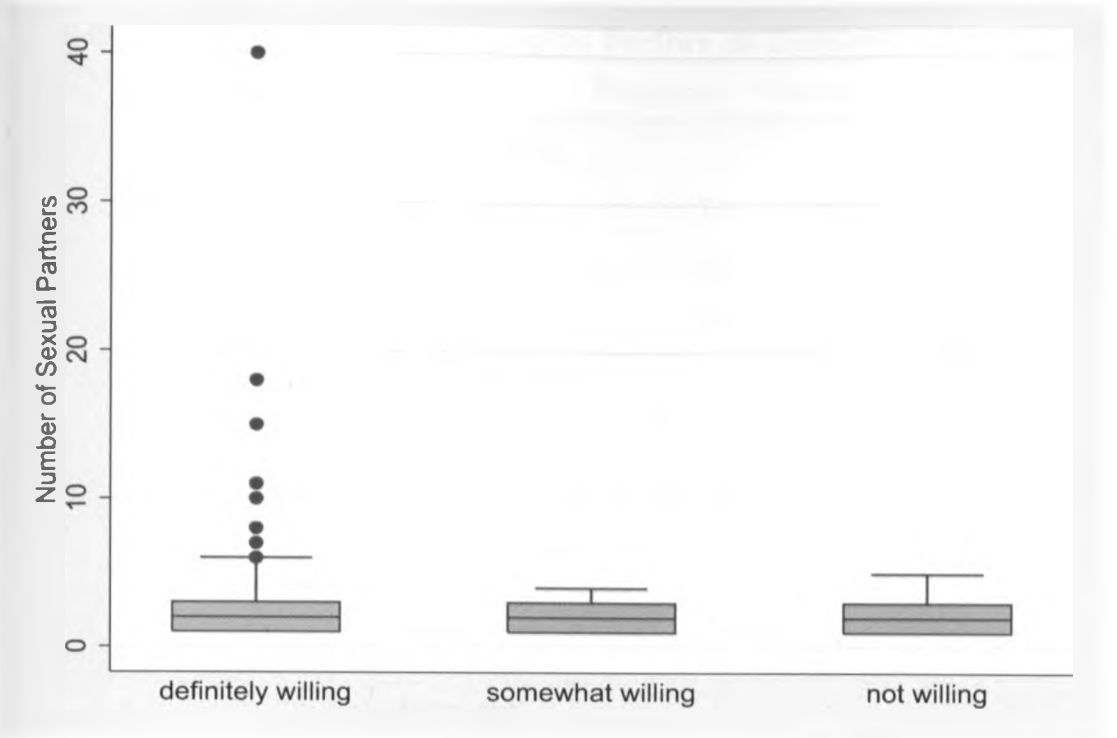

Figure 4.6: Box plot of number of sexual partners

Participants definitely willing to particpate in the vaccine trial had an average of 3 sexual partners compared to 2 for those not willing and somewhat willing.

Table 4.5: **Other Socio-Demographic Factors at Enrolment (Categorical)**

Factor	Frequency	Percent
Education level		
None	173	21.7
Primary	430	54.0
Secondary	154	19.3
Post-secondary	40	5.0
Marrital Status		
Married	709	89.0
Single	80	10.0
Windowed	3	0.4
Divorced	5	0.6
Employment		
Employed	277	34.8
Housewife	452	56.7
Unemployment	68	8.5

On average participants had acquired primary education (50%) while most of participants were married (94.2%) and for the form of employment number of housewives was above average (59.6%).

Table 4.6: **Knowledge of Vaccines, Microbicides and Clinical Trials**

Factor	Frequency	Percent
Knowledge of HIV prevention	765	96.0
Knowldge of Vaccines in general	43	5.4
Ever heard of vaccine against HIV	34	4.3

Among the study participants knowledge of the HIV prevention methods was quite high, with about 765 (96.0%) of the total participants. This included abstinence, faithfulness to one partner, treatment of STDs, use of condoms and reducing the numbuer of sexual partners one had. This was consistent with the previous studies where knowledge on the prevention was very high. In kenya, the high knowledge is as a result of the concerted campains and sensitization by

the Government. The knowledge of current vaccines in general was very low at 5.4% with even poorer knowledge on the continued works on the HIV vaccines and microbicides at 4.3%. This is basically due to the fact that most of the participants had primary education as compared to the previous study cohorts.

Table 4.7: **Attitude to Vaccine/Microbicides**

Factor	Frequency	Percent
How Effectiveness are the current vaccines against HIV?		
100%	131	16.4
75-99%	166	20.8
<75%	287	36.0
Don't know	213	26.7
Side effects of the current vaccines		
100%	24	3.0
75-99%	25	3.1
<75%	405	50.8
Don't know	343	43.0
Effectiveness of future vaccines		
100%	5	4.8
75-99%	6	5.8
<75%	57	54.8
Don't know	36	34.6
Future side effects of vaccines/microbicides		
100%	2	1.9
75-99%	5	4.8
<75%	75	72.1
Don't know	22	21.2

Attitude to vaccines and microbicides was also of concern and participants were assessed. 131 (16.4%) sited that the effectiveness of the current vaccines was 100%. 4.8% of the participants expected the future HIV vaccine to be 100%, which is a big draw back as this could dictate the participation levels of the participants. However, majority expected lower side-effects on the

future HIV vaccines at 72.1%.

Table 4.8: **Knowledge of Vaccines Over the Study Period**

Period [Time]	3m,(n=74)	6m,(n=55)	9m,(n=49)
Factors			
Knowledge of HIV prevention	74(100.0)	55(100.0)	49(100.0)
Ever heard of vaccines in General	74(100.0)	55 (100.0)	49(100.0)
Ever heard of HIV vaccines	49(66.2)	40(72.7)	48(98.0)

At month 3, all the participants had knowledge on the HIV prevention and had heard of vaccines in general. However, the knowledge on the HIV vaccine was at 66.2%. The knowledge on the HIV prevention remained high throught the remaining part of the study, as the participants were repeatedly asked on each visit amounting to the high knowledge on the vaccines.

Table 4.9: **Willingness to Participate in the Study Period**

Period [Time]	Enrol,(n=797)	3m,(n=74)	6m,(n=55)	9m,(n=49)
Vaccines/Microbicide				
Definitely willing	713(89.5)	62(83.8)	54(98.2)	47(95.9)
Some what willing	23(2.9)	5(6.8)	0	1(2.0)
Not willing	61(7.7)	7(9.5)	1(1.8)	1(2.0)

There was a high willingness to participate in the HIV/Microbicide trial with all the visits having report over eighty percent willingness.

4.3 Analysis and Results

Table 4.10: **Association Between the Baseline Factors and Willingness to Participate**

	Willingness				
Variable	Definitely	Somewhat	Not willing	F(df)	p-value
Age	24.0(0.2)	25.3(1.2)	24.3(0.6)	1.1(2,794)	0.323
Years in school	8.7(0.1)	8.9(0.7)	8.2(0.4)	1.3(2,794)	0.283
No.of Rooms	1.2(0.0)	1.1(0.1)	1.2(0.1)	0.7(2,794)	0.479
People in the room	3.21(0.1)	3.2(0.3)	3.5(0.2)	0.6(2,794)	0.526
Monthly Rent	1,634.3(35.4)	1,638(154.7)	1,723.7(145.2)	0.2(2,794)	0.780

There was no significant difference in means (age, years in school,no. of rooms, people in in the room and monthly rent) of the socio-demographic factors of the study participants across the willingness ($p - value > 0.05$).

Table 4.11: **Association Between Sexual History and Willingness to Participate**

	Willingness				
Variable	Definitely	Somewhat	Not willing	F(df)	p-value
Parity	2.2(0.0)	2.4(0.3)	2.4(0.2)	1.5(2,794)	0.233
Age at menarche	17.4(0.1)	17.8(0.6)	17.3(0.3)	0.2(2,794)	0.782
No.of sexual partners	2.5(0.1)	2.1(0.2)	2.2(0.1)	1.1(2,794)	0.335
Duration with current partner	4.2(0.1)	5.9(1.2)	4.5(0.6)	2.3(2,794)	0.099

There was no significant difference in the means in parity, age at menarche, number of sexual partners and the duration in which the participants had been with the current partners in years. (p-value >0.05).

Table 4.12: **Cross-tabs between Willingness and Socio-Demographic Factors, (Categorical)**

Factors	Overall Willingness				
	Definitely	Somewhat	Not willing	$\chi^2(df)$	p-value
Education level					
Primary and Below	60(78.9)	6(50.0)	12(75.0)	4.7(2)	0.099
Secondary and Above	16(21.1)	6(50.0)	4(25.0)		
Marrital Status					
Married	71(93.4)	11(91.7)	16(100.0)	3.8(2)	0.544
Single	5(6.6)	1(8.3)	0		
Employment Status					
Employed	24(31.6)	4(33.3)	9(56.3)	1.8(4)	0.376
Housewife	48(63.2)	7(58.3)	7(43.8)		
Unemployed	4(5.3)	1(8.3)	0		

Most participants who were definitely willing to participate in the study were married (82.2%), and had education level of primary and below (76.2%). However, there was no significant differences ($p - value > 0.05$).

Table 4.13: **Association Between Knowledge of Vaccines Trials and Willingness to Participate**

	Willingness				
Factor	Definitely	Somewhat	Not willing	$\chi^2(df)$	p-value
Knowledge of HIV prevention	686(96.2)	22(95.7)	57(93.4)	1.1(2)	0.569
Ever heard of Vaccines	34(4.8)	3(13.0)	6(9.8)	5.5(2)	0.063
Ever heard of HIV vaccines	31(4.3)	1(4.3)	2(3.3)	0.2(2)	0.924
Ever had STD	63(8.8)	4(17.4)	4(6.6)	2.5(2)	0.292

Most participants who were definitely willing to participate in the vaccine trial had a higher knowledge of HIV prevention at 96.2%. The knowledge on HIV prevention was quite high compared to the knowledge on vaccines and the HIV vaccines. The study participants had very limited knowledge on the vaccines, which could be explained by the socio-demographic factors and in particular owing to the fact that mojority had education level of primary and below.

Table 4.14: **Cross-tabs Between Willingness and Attitude to Vaccines**

Factors	Willingness				
	Definitely	Somewhat	Not willing	$\chi^2(df)$	p-value
Effectiveness of					
of Current Vaccines					
100%	15(19.7)	0	1(6.3)		
75 to 99%	18(23.7)	3(25.0)	3(18.8)	6.2(6)	0.396
≤75%	24(31.6)	6(50.0)	7(43.8)		
Don't know	19(25.0)	3(25.0)	5(13.3)		
Side-effects of the					
the current vaccines					
100%	1(1.3)	1(8.3)	1(6.3)		
75 to 99%	3(3.9)	0	1(6.3)	8.1(6)	0.229
≤75%	41(53.9)	5(41.7)	8(50.0)		
Don't know	31(40.8)	6(50.0)	6(37.5)		
Effectiveness of					
future vaccines					
100%	1(1.3)	1(8.3)	2(12.5)		
75 to 99%	5(6.6)	0	1(6.3)	3.1(6)	0.649
≤75%	43(56.6)	6(50.0)	8(50.0)		
Don't know	26(34.2)	5(41.7)	5(31.3)		
Side-effects of					
future vaccines					
100%	0	1(1.8)	1(6.3)		
75 to 99%	4(5.3)	0	1(6.3)	2.1(6)	0.125
≤75%	58(76.3)	6(80.0)	11(68.8)		
Don't know	14(18.4)	5(41.7)	3(18.3)		

Univariately, there was no significant association between the willingness to participate and the attitude of the participants, ($p - value > 0.05$).

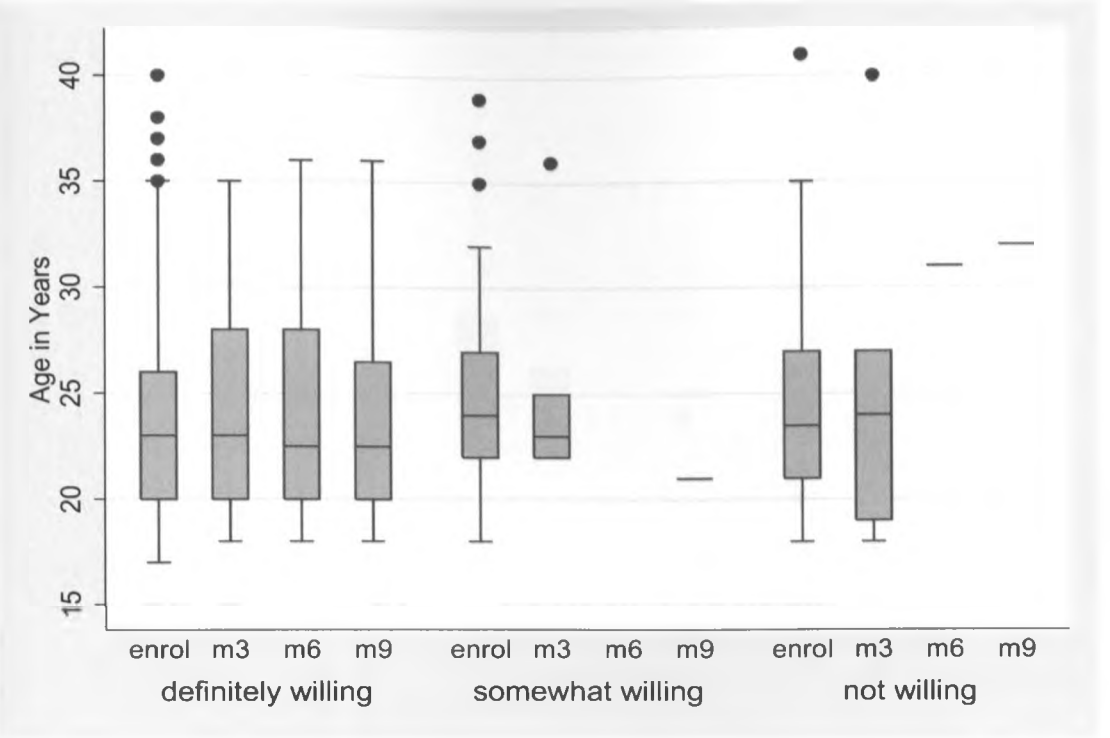

Figure 4.7: Comparison of the mean ages across the willingness to participate

Over the study period, the mean age of participants definitely willing to participate is 24.0, 24.2, 23.9 and 23.7 years at enrollment, month 3, month 6 and month 9 respectively. This indicated that there was no change in mean age over the follow-up period. For those participants who were somewhat willling to participate, their mean age was 25.3, 25.6 and 21.0 at enrollment, month 3, month 6 and at month 9 respectively. Mean age for those not willing to participate group differed significantly, with the early follow-up periods having a lower mean age (24.3) compared to the mean age at the later follow-up at 32.0 years of age. This is an indication that, older participants were likely to decline in participating in HIV vaccine trials.

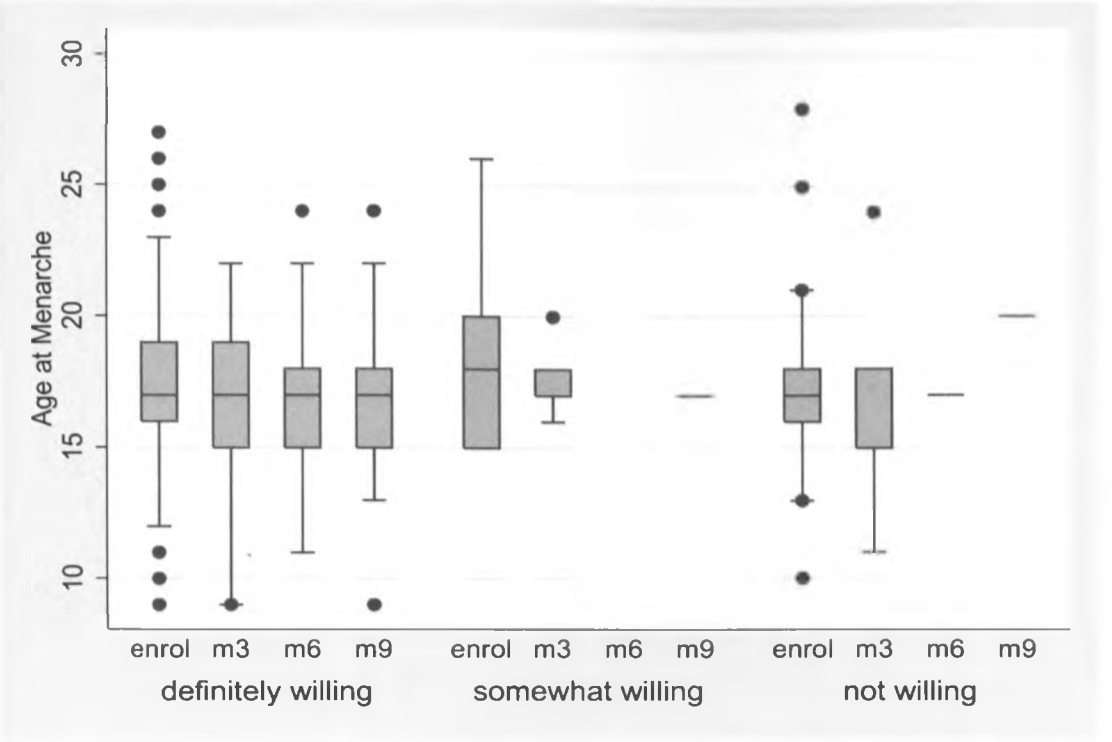

Figure 4.8: Comparison of the mean age at menarche across the willingness to participate

The mean age at menarche ranged between 17.5 at enrolment and 16.9 at month 9, a fairly constant average for the definitely willing group. For those participants with somewhat willing to participate, the mean age at menarche was the same at 17.8 years over the study follow-up period. Not willing to participate group had varied mean age at menarche with mean for those not willing to participate with a higher mean for of 20 years in month 9.

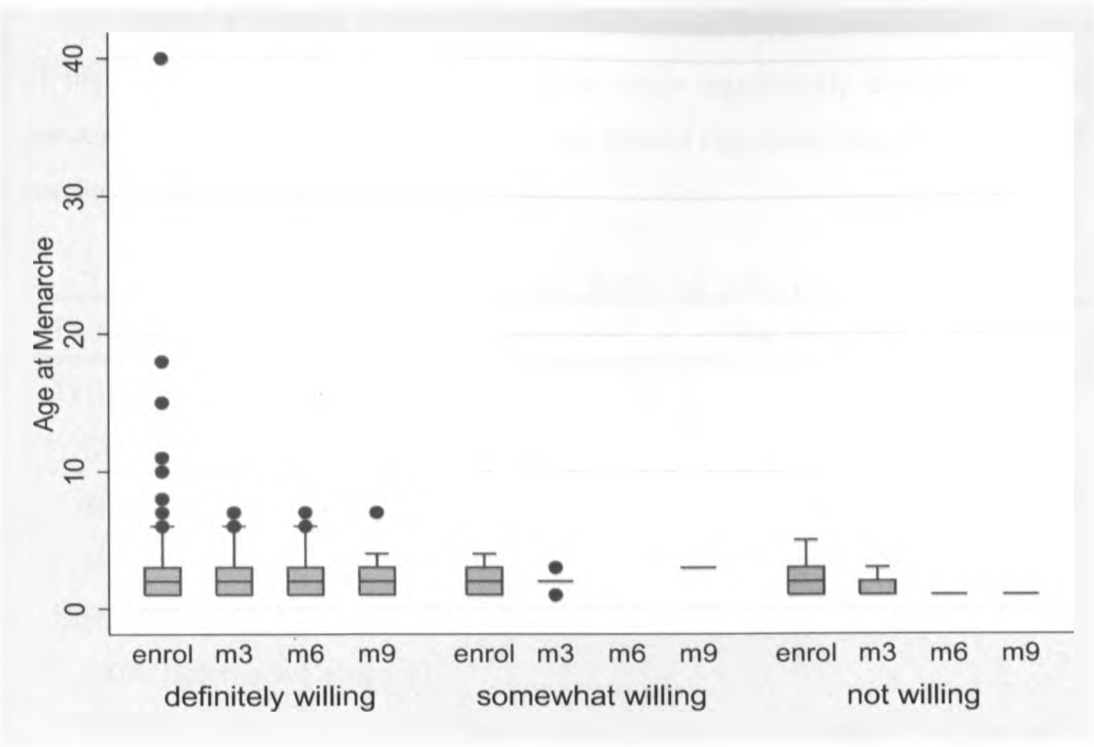

Figure 4.9: Comparison of the mean number of sexual partners across the willingness to participate

Those participants who were not willing to participate had less number of sexual partners (1.0) at month 9 compared to those at earlier study period with higher number of sexual partners on average (> 1). This could possibily be as aresult that participants with less partners felt less expossed hence the decline in participation.

On running a multiple ordered logistic, effectiveness of the current vaccines and side-effects of the current vaccines were the only factor which significantly explained the willingness to participate (see appendix II). In this case, the ordered regression analysis was carried out for the enrollment visit (n=797) only.

Table 4.15: **Table of Effects**

Factors	Par.Est.(SE)	95% CI	p-value
Willingness to Participate			
Definitely willing (Reference category)	-	-	-
Somewhat willing (1|2)	2.3(0.6)	0.7 to 3.5	0.001
Not willing (2|3)	2.7 (0.7)	0.6 to 4.0	0.003
Effectiveness of Current Vaccines			
100%(Reference Category)	-	-	-
75-99%	0.5(0.7)	-1.2 to 0.7	0.023
<75%	0.6(0.4)	-1.0 to 0.8	0.185
Don't know	1.1(0.4)	0.3 to 2.1	0.185
Side-Effects of Current Vaccines			
100%	(Reference Category)	-	-
75-99%	0.6(0.8)	-0.8 to 1.8	0.451
<75%	-0.5(0.6)	-0.2 to 2.4	0.016
Don't know	-0.6(0.7)	-0.2 to 0.6	0.969

On running the FULL (see appendix II) model the only effectiveness of the current vaccines and side-effects of the current vaccines resulted as only significant factors in modelling willingness to participate in the HIV vaccines. The intercept (ordered responses) was also significant ($p-value < 0.05$).

The FULL model fitting information is displayed in table (4.16) and Goodness-of-fit in table (4.17) below,

Table 4.16: **Model Fitting Information of Full Model**

Model	2Log.Likelihood	χ^2	*df*	Sig.
Intercept	610.70			
Final	574.70	35.90	23	0.042

Table 4.17: **Goodness-of-Fit of Full Model**

	χ^2	*df*	Sig.
Pearson	1,507.6	1,497	0.419
Deviance	574.7	1,497	1.000

THE **AIC** OF THE FULL-MODEL = 640.04

The REDUCED model fitting information is displayed in table (4.18) and Goodness-of-fit table (4.19) below,

Table 4.18: **Model Fitting Information for the Reduced Model**

Model	2Log.Likelihood	χ^2	*df*	Sig.
Intercept	87.4			
Final	76.0	11.4	6	0.077

Table 4.19: **Goodness-of-Fit of the Reduced Model**

	χ^2	*df*	Sig.
Pearson	14.7	24	0.930
Deviance	15.4	24	0.908

THE AIC OF THE REDUCED-MODEL $= \underline{\underline{639.44}}$

This is the Model with least AIC.

4.4 Model Adquacy Testing

To test the adquacy of the Model we use the likelihood ratio statistic defined as

$$\begin{aligned} D &= 2\log\lambda \\ &= 498.7 \\ &= \underline{\underline{499}} \end{aligned} \tag{4.1}$$

We compare

$$\begin{aligned} D &< \chi^2_{(774,0.05)} \\ 499 &< 853. \end{aligned} \tag{4.2}$$

and conclude that the model is **CORRECT** at α-level of $= 0.05$ since D$< \chi^2_{n-p,\alpha}$

The Model,

$$\log\left(\frac{P_2}{P_1}\right) = 2.3(\pm 0.6) + 0.5(\pm 0.7) \times (75 - 99)\% - 0.5(\pm 0.6) \times (< 75)\% \qquad (4.3)$$

and

$$\log\left(\frac{P_3}{P_2}\right) = 2.7(\pm 0.7) + 0.5(\pm 0.7) \times (75 - 99)\% - 0.5(\pm 0.6) \times (< 75)\% \qquad (4.4)$$

Chapter 5

Conclusions and Recommendations

5.1 Conclusions

1. Willingness to participate in the HIV vaccine trial was high over the study period.
2. Knowledge of HIV/AIDS prevention among the study participants was high however, the knowledge of vaccines in general and HIV vaccines was very low in the study participants,
3. Factors associated with the willingness to participate in the study are, the effectiveness of the current vaccines and their side-effects.

5.2 Recommendations

1. More sensitization on vaccines in general is needed and more importantly the current HIV vaccine initiatives.
2. The performance of the current vaccines is key to future vaccine developments and their side-effects need to be minimized for better results for enhanced participation in future vaccine trials.

APPENDICES

Appendix I: Study Questionnaire

Study Questionnaire - Enrollment

Study Number.....

A. Socio-Demographic Data

Age, Years of Schooling, Highest level of education, Marital Status, Employment, Number of rooms, How many people live in your house, Monthly salary.

B. Knowledge of Vaccines, microbicides and clinical trials

1. How can sexual trasmission of HIV be prevented?
2. Have you ever heard of a vaccine?
3. Which diseases do you know of vaccines against?
4. Have you ever heard of a vaccine against HIV?
5. What have you heard about vaccines against HIV?
6. Have you ever heard of substances capable of killing or neutralizing viruses and bacteria that may be applied into the vagina before intercourse (Microbicides)?
7. Have you ever heard of a microbicide to prevent HIV transmission?

8. If yes, what have you heard about microbicides to prevent HIV transmission?

9. If you participated in a trial to test whether a vaccine works, Scientists should know whether it will work or not before the study

10. You may receive the vaccine or substance that has no effect?

11. The decision of whether you receive the vaccine or not should be made at random?

12. You should know whether you are receiving the vaccine or not?

13. The scientists should know whether you are receiving the vaccine or not?

C. Attitudes to vaccines and microbicides

14. How many times out of a 100 do you think currently available vaccines prevent diseases?

15. How effective do you think vaccines against HIV will be (Prompt)?

16. How many times out of 100 do you think currently available vaccines have side-effects?

17. How often do you think that a HIV vaccine will have side effects? (Prompt)

18. How many times out of a 100 do you think a microbicides against HIV will be effective?

19. How many times out of a hundred do you think a microbicide against HIV will have side effects?

20. Will using condoms be necessary if an effective microbicide against HIV was available?

D. Willingness to participate

21. How willing would you be to take part in a study that required you to receive a vaccine to test if it protects against HIV? (Prompt)

22. If not willing, why? Fear of:-

23. If willing, why?

24. How willing would you be to take part in a study that you used a microbicide to test if it protects against HIV? (Prompt)

25. If not willing, why? Fear of:-

26. If willing, why?

27. If not willing, why not? Fear of:How willing would you be to receive a safe and effective HIV vaccine if it was available? (prompt)

28. How willing would you be to use an effective microbicide against HIV if it was available? (Prompt)

29. If not willing, why not? Fear of:-

E. Sexuality

30. How many pregnancies have you had

31. At what age did you first have sexual relations?

32. How many sexual partners have you had in your life?

33. Have you ever had a STD (syphilis, gonorrhea, genital ulcers or warts)?

34. How many sexual partners have you had in the last 1 year, other than your regular partner

35. If yes, were they? (Prompt)

36. How long have you been with your current partner

37. Do you think your partner has other sexual partners?

38. Do you feel you may have been at risk of HIV infection in the last 1 year?

39. Do you use condoms with your:-

40. If yes, how often do you use condoms with you regular partner? (Prompt)

41. If yes how often do you use condoms with other partners?(Prompt)

Follow-up Questionnaire

Study Number .....

A. Knowledge of Vaccines, microbicides and clinical trials

1. How can sexual transmission of HIV be prevented?
2. Have you ever heard of a vaccine?
3. If yes, what is a vaccine for? (Tick one)
4. Which diseases do you know of vaccines against ?
5. Have you ever heard of a vaccine against HIV?
6. What have you heard about vaccines against HIV?
7. Have you ever heard of substances capable of killing or neutralizing viruses and bacteria that may be applied into the vagina before intercourse (Microbicides).
8. If yes, what are they used for?
9. Have you ever heard of a microbicide to prevent HIV transmission?
10. If yes, what have you heard about microbicides to prevent HIV transmission?
11. If you participated in a trial to test whether a vaccine works, Scientists should know whether it will work or not before the study?
12. You may receive the vaccine or substance that has no effect?
13. The decision of whether you receive the vaccine or not should be made at random?
14. You should know whether you are receiving the vaccine or not?
15. The scientists should know whether you are receiving the vaccine or not?

B. Willingness to Participate

16. How willing would you be to take part in a study that required you to receive a vaccine to test if it protects against HIV? (Prompt)
17. If not willing, why? Fear of:-
18. If willing, why?
19. How willing would you be to take part in a study that you used a microbicide to test if it protects against HIV? (Prompt)
20. If not willing, why? Fear of:-
21. If willing, why?
22. If not willing, why not? Fear of:How willing would you be to receive a safe and effective HIV vaccine if it was available? (prompt)
23. How willing would you be to use an effective microbicide against HIV if it was available? (Prompt)
24. If not willing, why not? Fear of:-

C. Sexuality

25. How many pregnancies have you had
26. At what age did you first have sexual relations?
27. How many sexual partners have you had in your life?
28. Have you ever had a STD (syphilis, gonorrhea, genital ulcers or warts)?
29. How many sexual partners have you had in the last 1 year, other than your regular partner
30. If yes, were they? (Prompt)
31. How long have you been with your current partner
32. Do you think your partner has other sexual partners?

33. Do you feel you may have been at risk of HIV infection in the last 1 year?

34. Do you use condoms with your:-

35. If yes, how often do you use condoms with you regular partner? (Prompt)

36. If yes how often do you use condoms with other partners?(Prompt)

Appendix II: Output of the Results

```
==========================================================================
> library(nnet) # For polytomous logistic regression
> library(MASS) # For ordinal logistic regression
==========================================================================
> class(intense) # "factor"
> intense.ord <- ordered(intense)
> class(intense.ord) # "ordered" "factor"
> ord.hw <- polr(intense.ord ~ agegr + shoes)
> summary(ord.hw)
==========================================================================
> ordinal.or.display(ord.hw)
Ordinal OR lower95ci upper95ci P.value
agegr15-59 yrs 2.169 1.517 3.116 1.39e-05
agegr60+ yrs 3.596 1.913 6.788 4.07e-05
shoesyes 0.485 0.341 0.686 2.71e-05
==========================================================================
CROSSTABS
  /TABLES=KNOWLEDGEonHIVPrevention HEARDOfVaccineinGENERAL HEARDofVaccineinHIV
  BY WillingnesstoParticipat1
  /FORMAT= AVALUE TABLES
  /STATISTIC=CHISQ
  /CELLS= COUNT COLUMN
  /COUNT ROUND CELL .
==========================================================================
CROSSTABS
  /TABLES=std1  BY WillingnesstoParticipat1
  /FORMAT= AVALUE TABLES
  /STATISTIC=CHISQ
  /CELLS= COUNT COLUMN
```

```
  /COUNT ROUND CELL .
=============================================================================
CROSSTABS
  /TABLES=KNOWLEDGEonHIVPrevention HEARDOfVaccineinGENERAL HEARDofVaccineinHIV
  BY WillingnesstoParticipat1
  /FORMAT= AVALUE TABLES
  /STATISTIC=CHISQ
  /CELLS= COUNT COLUMN
  /COUNT ROUND CELL .
CROSSTABS
  /TABLES=std1  BY WillingnesstoParticipat1
  /FORMAT= AVALUE TABLES
  /STATISTIC=CHISQ
  /CELLS= COUNT COLUMN
  /COUNT ROUND CELL .
FREQUENCIES
  VARIABLES=M2KnoledgeonHIVPrevention m3HeardofVACCINE HeardofHIVvaccine
   _Microbicide
  /FORMAT=NOTABLE
  /STATISTICS=SEMEAN MEAN
  /ORDER=  ANALYSIS .
FREQUENCIES
  VARIABLES=M9HIVprevention m9HeardofVaccine m9heardHIVvaccine
  /ORDER=  ANALYSIS .
=============================================================================
attach(w)
WILL2=as.ordered(WILL)
> ED=as.factor(ED)
> age=as.factor(age)
> marit=as.factor(marit)
> emplo=as.factor(emplo)
```

```
> nnple=as.factor(nnple)
> HIVknow=as.factor(HIVknow)
> HEARDvacGen=as.factor(HEARDvacGen)
> HEARDofVacc=as.factor(HEARDofVacc)
> EffCurent=as.factor(EffCurent)
> SideEFFcurr=as.factor(SideEFFcurr)
> Parity=as.factor(Parity)
> Menr=as.factor(Menr)
> STD=as.factor(STD)
> Duration=as.factor(Duration)
```

==========

```
Re-fitting to get Hessian

Call:
polr(formula = WILL2 ~ ED + age + marit + emplo + nnple + HIVknow +
    HEARDvacGen + HEARDofVacc + EffCurent + SideEFFcurr + Parity +
    Menr + STD + Duration)

Coefficients:
                    Value   Std. Error       t value
ED.L           0.14518094 1.996871e-01  7.270423e-01
age2          -0.02735294 3.815595e-01 -7.168721e-02
marit2        -1.09828820 7.327040e-01 -1.498952e+00
marit3       -12.57569789 4.912139e-07 -2.560127e+07
marit4         0.41473500 1.171367e+00  3.540607e-01
emplo2        -0.11211734 2.578213e-01 -4.348645e-01
emplo3        -0.12270040 6.643502e-01 -1.846923e-01
nnple2        -0.23856023 3.123244e-01 -7.638219e-01
HIVknow2       0.29584630 5.292289e-01  5.590139e-01
HEARDvacGen1   1.53123250 5.036105e-01  3.040510e+00
HEARDofVacc1  -1.44072291 7.705799e-01 -1.869661e+00
EffCurent2     0.59835864 4.719428e-01  1.267863e+00
```

```
EffCurent3     0.63039079 4.307957e-01  1.463317e+00
EffCurent4     1.05205967 4.583177e-01  2.295481e+00
SideEFFcurr2   0.63050230 8.221609e-01  7.668843e-01
SideEFFcurr3  -0.65450387 6.709919e-01 -9.754274e-01
SideEFFcurr4  -0.64738549 6.811435e-01 -9.504392e-01
Parity2        0.06488404 3.396941e-01  1.910073e-01
Menr2         -0.25305582 2.486864e-01 -1.017570e+00
STD1          -0.13124551 4.156422e-01 -3.157656e-01
Duration2      0.28099884 2.961776e-01  9.487510e-01

Intercepts:
    Value         Std. Error    t value
0|1  2.062900e+00  7.444000e-01  2.771200e+00
1|2  2.429100e+00  7.473000e-01  3.250400e+00

Residual Deviance: 605.6193
AIC: 651.6193
================================================================================
STEP
Re-fitting to get Hessian
Call:
polr(formula = WILL2 ~ EffCurent + SideEFFcurr)
Coefficients:
                  Value Std. Error    t value
EffCurent2    0.5178655  0.4586583  1.1290879
EffCurent3    0.6245307  0.4232349  1.4756124
EffCurent4    1.0601494  0.4502341  2.3546627
SideEFFcurr2  0.6462799  0.7991772  0.8086816
SideEFFcurr3 -0.5221413  0.6567397 -0.7950506
SideEFFcurr4 -0.5947025  0.6669346 -0.8916954
```

```
Intercepts:
    Value   Std. Error t value
0|1  2.3081  0.6669     3.4611
1|2  2.6651  0.6702     3.9768

Residual Deviance: 624.0441
AIC: 640.0441
> step(ord.hw)
Start:  AIC=640.04
WILL2 ~ EffCurent + SideEFFcurr

              Df    AIC
- SideEFFcurr  3 639.44
<none>           640.04
- EffCurent    3 640.44

Step:  AIC=639.44
WILL2 ~ EffCurent

            Df    AIC
<none>         639.44
- EffCurent  3 639.44
Call:
polr(formula = WILL2 ~ EffCurent)

Coefficients:
EffCurent2 EffCurent3 EffCurent4
 0.5657735  0.5529527  0.9358397

Intercepts:
     0|1      1|2
```

2.738570 3.092495

Residual Deviance: 629.4373

AIC: 639.4373

==========

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