UNIVERSITY OF GOTHENBURG
SCHOOL OF BUSINESS, ECONOMICS AND LAW

Patient Adherence to Antiretroviral Therapy and its Relationship to Food Insecurity

A Study in the uMgungundlovu District of KwaZulu Natal, South Africa

Mia Lindgren, Autumn 2016
Bachelor's Thesis (15 hp)

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With an expanding programme for antiretroviral therapy (ART) in South Africa and other countries following new guidelines and goals from the World Health Organization and UNAIDS, it's as important as ever to understand the barriers that exists for this treatment to be successful. This thesis investigates how economic vulnerability in the form of food insecurity affects adherence to treatment among HIV positive individuals on antiretroviral therapy in the uMgungundlovu District of KwaZulu Natal in South Africa. An increasing amount of literature identifies food insecurity as an important barrier to treatment adherence among people living with HIV (PLHIV) and this study has investigated if this is also the case in a region of South Africa that is highly resource restrained and where there is a high prevalence of HIV. Cross sectional data from a large study where over 10 000 people were interviewed was used, where food insecurity was reported on a household level and HIV positive respondents answered questions on adherence to treatment. Univariate and multivariate logistic regressions were run, finding significantly lower odds of adhering to ART when suffering from the highest degree of food insecurity (Multivariate analysis: O.R.=0.42, $p<0.05$). This thesis identifies members of the most severely food insecure households as a key population where nutritional support might positively affect adherence and thereby aid in the success of treatment programmes.

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List of abbreviations

AIDS	Acquired Immunodeficiency Syndrome
ART	Antiretroviral Therapy
ARV's	Antiretroviral Drugs
CASE	Center for Adherence Support Evaluation
CES-D	Center for Epidemiologic Studies Depression Scale
CI	Confidence Interval
FAAI	Food Adequacy Access Index
HIV	Human Immunodeficiency Virus
NSNP	National School Nutrition Programme
O.R.	Odds Ratio
PDA	Personal Digital Assistant
PLHIV	People Living with HIV
RUTF	Ready-to-Use Therapeutic Food
Stats SA	Statistics South Africa
UNAIDS	Joint United Nations Programme on HIV/AIDS
UTT	Universal Test and Treat

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1. Introduction

In this chapter the subject of this essay, adherence to antiretroviral treatment (ART) and food insecurity will be discussed after briefly introducing the topics of HIV and treatment policies and guidelines. It should hopefully become apparent that HIV treatment is a topic that is not only relevant for research in the fields of medicine and global health, but also highly relevant for economic research.

Human immunodeficiency virus (HIV) is a virus that breaks down the immune system of infected individuals. The virus infects cells of the immune system, leading to a depletion of such cells, especially the so called CD4 positive T cells. Untreated, this will over time lead to a secondary immunodeficiency referred to as acquired immunodeficiency syndrome (AIDS). This is a condition where opportunistic infections and secondary cancers develop, causing severe and life-threatening disease. The virus also attacks the central nervous system, leading to neurological manifestations (Kumar et al. 2010). Since the first case in the 1980s (Murphy 2012), HIV/AIDS has spread across the globe. The Joint United Nations Programme on HIV/AIDS (UNAIDS) estimates that nearly 37 million people are infected by the virus (UNAIDS 2016a), causing tremendous suffering and affecting whole economies in highly affected countries (Haacker 2004).

Today a lot is being done to fight HIV/AIDS worldwide. Effective treatment regimens that hinder development of AIDS exist, and over the last 15 years, the world-wide number of people reached by treatment has increased to over 40% (UNAIDS 2016a). As part of the United Nations Sustainable Development Goals, ambitious targets have been set by UNAIDS which includes increasing this number further. The important 90-90-90-goal states that 90% of people with HIV should know their status, 90% of these people should receive treatment and 90% of people on treatment should have supressed viral loads by the year 2020 (UNAIDS 2015).

In South Africa, an approximated seven million people live with HIV, making it one of the most highly affected countries globally (UNAIDS 2016b). It is also one of the countries that are leading the way in an attempt to reach the UNAIDS goals. For example, in September 2016 South Africa switched to a system of Universal Test and Treat (UTT). This means that everyone testing positive for HIV can be enrolled onto antiretroviral therapy (ART) regardless of CD4 count and how far their illness has progressed. This has the possibility of creating a series of positive effects and directly supports the UNAIDS 90-90-90 target. However, as the South African Department of Health recognizes; *"*Key to success of Universal Test and Treat

is implementation of the National Adherence Policy and service delivery guidelines interventions for linkage to care, adherence to treatment and retention in care*"* (Pillay & Pillay 2016).

The purpose of this thesis is to examine the adherence rates to ART among people living with HIV (PLHIV) in a high HIV-prevalence area in South Africa and examine whether experiencing a lack of food will influence the likelihood of adhering to treatment. Food insecurity is in this thesis seen as a possible barrier that could negatively influence the effectiveness of public spending on ART. Analysis is done using data collected in a cross-sectional study where over 10 000 inhabitants of the uMgungundlovu District in KwaZulu Natal were interviewed and tested for HIV. Regression analysis is used to investigate the possibility of a causal relationship or correlation between adherence to treatment and food insecurity. The research hypothesis is that food insecurity has a negative effect on adherence to ART.

The topic of this thesis is of interest since reaching high levels of treatment adherence is very important. High levels of adherence will aid in achieving both viral suppression and increasing CD4 counts (Aibibula et al. 2016, Mannheimer et al. 2006). This in turn predicts longer life and can keep the disease from progressing into AIDS (Bangsberg et al. 2001, Lewden et al. 2007). High levels of adherence will further reduce the risk of both horizontal and vertical spread of the virus (Cohen et al. 2011, WHO 2010). A third important reason for why adherence is a very important subject is that of drug resistance. With sub-optimal adherence, the risk of resistant strands of the virus developing increases (Sethi et al. 2003, Tam et al. 2008, Meresse et al. 2014). Adherence is therefore important to analyse and promote.

A lot of research has been conducted with a focus on the barriers to ART adherence, and food insecurity has been identified as one such barrier. Food insecurity is a poverty related factor that can be seen as one of the several structural barriers (Kagee et al. 2011). Other important factors found in research conducted in Southern Africa include problems with access to transportation to clinics and lost wages for day labourers. Along with stigma, gender inequalities and inadequate institutions this will lead to people dropping out of treatment or failing to adhere properly to their medical regimens (Kagee et al. 2011). Individual level factors and household level factors are also of importance. For example, type of dosing schedule and experienced or anticipated side effects have proven relevant for adherence (Mills et al. 2006a), as well as unstable housing and lack of family support (Young et al.

2014). Although there are many factors at play, this study will, as explained, be limited to examining the role of food insecurity on HIV treatment adherence.

There is a growing amount of studies pointing towards the importance of food insecurity for adherence to ART and health outcomes for PLHIV. In a recent systematic review nine articles out of 13 found a statistically significant relationship between sub-optimal adherence and being food insecure (Singer, Weiser & McCoy 2015). This connection is also supported and clarified by qualitative research on the topic. In a review, Young et al. (2014) summarized four pathways through which food insecurity can impede adherence to ART: 1) Fear of and actual experiences of worsened side effects of the medication. 2) Increased hunger when taking ART was also reported as a reason for not taking the antiretroviral drugs (ARV's). 3) Additionally, there can be issues of trade-offs between buying food and paying for medicines or transport to medical facilities where medicines are collected. 4) Lack of money for food there is also a risk of PLHIV choosing to sell medicines instead of taking them, adding to the vulnerability of food insecure people, even in a setting where medicines are free and easily available (Young et al. 2014). In a recent article, Whittle et al. (2016) also described how food insecurity could affect adherence through the effect it had on respondents' psychological well-being. Food insecurity was found to interact with or lead to depression or depressive symptoms. This in turn would have a negative effect on adherence by hindering a regular routine and leading to missed clinical appointments. Depression would therefore at least in part, be a mediator for poor adherence among people suffering from food insecurity.

Apart from the observed relationship between food insecurity and adherence, the possibility of a connection between food insecurity and other health determinants has also been researched. A meta-analysis recently found that people suffering from food insecurity had on average 91 fewer CD4 cells/µl than food secure people living with the virus (Aibibula et al. 2016). Food insecurity has also been connected to poorer virologic response among PLHIV on ART (Kalichman et al. 2015, Wang et al. 2011). As Kalichman et al. (2015) highlights, some ARV's are supposed to be taken with food in order to be processed and absorbed optimally. A lack of food in the household is therefore something that can both affect adherence and treatment outcomes even if adherent to medication.

Even though the hypothesis of a negative relationship between food insecurity and adherence to ART is supported by earlier research, there is reason to investigate this topic further. Study designs vary and several studies only find significant results before controlling for omitted variables, or lack multivariate analysis (Aibibula et al. 2016, Singer, Weiser & McCoy 2014).

This could cause omitted variable bias. One study actually found that adherence rates were higher among people that reported food insecurity (Sasaki et al. 2012). However, the researchers reasoned in the article that this might have been due to a form of response bias. This thesis will, as mentioned, retest the argument that food insecurity has a negative effect on ART adherence in a South African setting where HIV prevalence is high. With an expanding ART programme in South Africa, food assistance programmes might also be needed to achieve optimal health outcomes.

The main finding of this thesis is that severe food insecurity does have a significant negative effect on adherence to ART. This relationship is however only observed among respondents that reported the highest level of household food insecurity. The most vulnerable part of the society is therefore identified as a key population where food insecurity seems to negatively influence adherence to ART. Indications that nutritional support was helpful for this group was also observed, although this effect of nutritional support was not significant when adding further control variables.

The outline of the rest of this thesis is as follows: In the ensuing theory section, the economic concept of time discounting is introduced and the theory of hyperbolic discounting will be used to help understand why a relationship could exist between level of adherence to ART and food insecurity. This theory gives an appealing explanation for health behaviour and has been found relevant for understanding health behaviour (Bleichrodt, Gao & Rohde 2016, Ikeda, Kato & Ohtake 2016, Pauly, McGuire & Barros 2011). This is followed by a data section where the survey and data collection is introduced and the variables and models are explained. The data chapter ends with a section where descriptive statistics are presented through graphs and tables. This section will give an overview of the data collected, and an extra focus is given to the high adherence rates found in this study. The results mentioned above are presented through regression tables and discussed in a results and discussion chapter. Since nutritional support was found to be an important variable to control for, research and visits to clinics and a school in the area was also conducted to get a better understanding of what types of nutritional support was accessible in the area. This information is presented at the end of the results and discussion chapter. Lastly the conclusions drawn from the results will be summarized, mentioning certain limitations that should be considered.

2. Theory

In this chapter, a time preference theory called hyperbolic discounting is introduced to illustrate how food insecurity possibly could lead to lower ART adherence levels through so called preference reversals. This theory introduces the concept of how different individuals will invest different amounts of time and money in their future health and that these preferences can change over time.

2.1 Discounting time and costs of adhering to ART

The concept of utility is central to how people make choices. In the world of economics, it is often assumed that human beings are rational people who, when given a choice of how to spend money and time, will choose the option that gives the highest utility. This also relates to choices we make when it comes to our health, such as the choice of adhering to a treatment regimen or not. Adhering comes with both costs and benefits, and typically, the costs are in the present, while the reward - future good health - is received at a later point in time. Such a choice, with trade-offs involving possible costs and benefits occurring at different points in time is called an intertemporal choice (Frederick, Loewenstein & O'Donoghue 2002). Theory on intertemporal choices can illustrate how reasons found in qualitative research, discussed above, could lead to lower adherence among food insecure individuals, through a reversal of adherence preferences.

Costs of adhering to ART do not only include monetary costs, but also opportunity costs and side effects. Monetary costs of adhering to treatment include the cost of pills, but could also, as Young et al. acknowledges (2014), include costs such as transportation to the clinic for picking up pills. For everyone to be able to afford treatment, ART is heavily subsidized in South Africa and in the group studied in this paper, only 24 people out of 2200 reported paying for their medicines (10-2500 ZAR). However, costs for transportation and other related costs could still occur. Opportunity costs include potentially foregoing other economic opportunities when presenting at the clinic for medication. If the clinic is far away and the wait at the clinic is long, then the possibility of working that day is lost. Equally, there might occur side effects from the medication that will make it difficult to work after taking them. Another type of opportunity cost of taking ones' medicines is the lost income that could otherwise have been earned by selling the ARV's on the black market[1]. These are a couple of possible opportunity costs that would be more difficult to take for a highly resource-restricted family, where the cost to adhering to ART might be to not afford food in the present. Exacerbated side effects and increased hunger when taking ART without having proper

[1] ARV's can be used as drugs and smoked for recreational purposes.

access to food are also costs that comes in the present and have been acknowledged as reasons for not adhering when experiencing food insecurity (Young et al. 2014).

According to economic theory and research, we normally discount future utility and therefore value utility received in the present higher. How much we discount the future will be influenced by an individual's time preference (how much a utility received in the present is preferred over a delayed utility), but also by uncertainty about the future and the possibility of changed preferences in the future (Frederick, Loewenstein & O'Donoghue 2002). Someone that is food insecure and experiences uncertainty about the future might therefore discount future health more than someone with less uncertainty about the future, apart from experiencing higher costs in the present.

Different time discounting theories exist, including models of constant discounting (where the discount factor is constant and the same for all time periods), quasi-hyperbolic discounting and hyperbolic discounting (Bleichrodt, Gao & Rohde 2016). Models of hyperbolic discounting has received more attention since the first models of constant discounting came and economic research indicates that they might have a better explicatory value for human behaviour, including health behaviour, than models of constant discounting (Frederick, Loewenstein & O'Donoghue 2002, Bleichrodt, Gao & Rohde 2016). This model can also add value and understanding to a possible relationship between food insecurity and degree of ART adherence and will be described below.

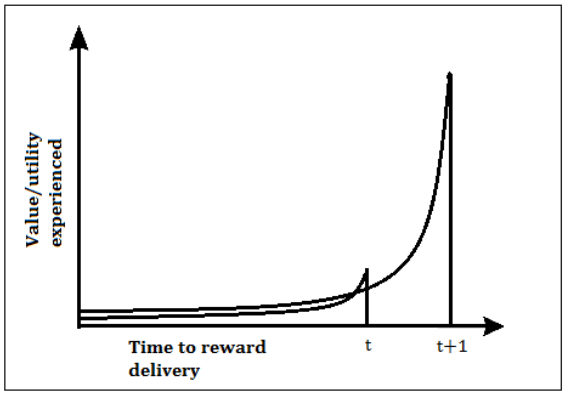
2.2 Hyperbolic discounting

Hyperbolic discounting is an economic theory of time discounting that has a focus on time inconsistencies. According to this theory, what we prefer to do at a specific time, t, will vary between time periods. A model for hyperbolic discounting in regards to adherence to ART has been constructed by Cobus Burger and can be viewed in his paper (n.d.). As Burger points out, the costs of adhering to treatment are normally experienced in the present, whereas the health benefits are experienced over time. At the onset of therapy, the patient might have the ambition to take all tablets as prescribed, and values this option higher than not taking the medications as prescribed. However, as time goes by, a point in time might come when the current costs of taking the medicines seem higher than the future benefits that could come from perfect adherence. A decision of skipping one or a few dosages might therefore be preferred in the present, while high adherence is still preferred for the coming time periods. This is an example of time inconsistency, and it will reappear in the following time periods if the circumstances are similar. If a lack of food is still an issue in the next time period, the

patient will once again see a short-run benefit of not adhering and since the future utility is discounted, opt for a lower adherence level than previously envisioned. Someone who exhibits this type of hyperbolic discounting-behaviour will therefore risk opting for a short term, lower benefit, instead of the larger, long term benefit of perfect adherence. The theory of hyperbolic discounting thus supports the hypothesis that PLHIV suffering from food insecurity will have a lower probability of adhering to treatment.

This human behaviour has also been described by Gowdy, Rosser and Roy (2013). They illustrate how the short-term, smaller benefit is preferred temporarily, just before it is accessible, whereas both before that time and looking back afterwards, the larger but delayed reward would be the preferred one. This is illustrated in the same way in figure 1, where a person just before time t, will change preferences and opt for a smaller reward that can be received in the present.

FIGURE 1. TIME INCONSISTENCIES IN HYPERBOLIC DISCOUNTING



Ikeda, Kato and Ohtake (2016) as well as Frederick, Loewenstein and O'Donoghue (2002) however also acknowledges that losses generally are discounted less than gains. This is denoted *the sign effect*. Ikeda, Kato and Ohtake refer to a study where individuals were indifferent between receiving $100 now and $157 in a year and indifferent between losing $100 now and losing $133 in a year. We seem less willing to delay losses than to push gains forward in time, exhibiting lower discount rates for losses than for gains. If displaying a sign effect, a greater deal of costs will therefore be accepted in the present in order to avoid future bad health outcomes. The existence of a sign effect does not contradict the hypothesis of this thesis. However, as long as patients are well informed of the risks that comes with not adhering to ART treatment, it can lead to a weaker relationship between food insecurity and non-adherence than a model of hyperbolic discounting that does not take the sign effect into consideration would estimate.

3. Data & Analysis

Divided into nine sections, this chapter will give an insight into study design and the population and sample studied. It will also describe the method of analysis and the different variables included. The main variables are described in more detail and at the end of the chapter, summary statistics are presented to give an overview of population characteristics and survey responses.

3.1 Cross-sectional survey data

The data analysed in this thesis comes from a big cross-sectional survey carried out in rural, informal and peri-urban settings of the uMgungundlovu Municipality in KwaZulu Natal, South Africa. This survey was part of a longitudinal study with the main purpose of establishing population HIV incidence and prevalence rates in the area. The longitudinal study consists of two cross-sectional surveys where HIV-negative individuals at baseline are followed up to establish a measure of incidence. However, apart from HIV-testing participants were asked a series of questions including general demographic questions and HIV-related questions. It is information retrieved from these interviews that is used in this analysis.

That the data collected is reliable and representative for the population is important. To reduce the risk of any bias in the sample, the data was collected through the randomised selection of households and respondents. Weights were added and all data was controlled for clustering to ensure data and results were representative of the area. In appendix A1, the data collection process is described in more detail and for a description of the overall study design, see; Kharsany et al. (2015), under references.

3.2 Approach/logistic regression analysis

To investigate if a correlation and possible causal relationship between food insecurity and adherence to ART exists, several logistic regressions were run with regression results reported as odds ratios. Logistic regression is a good method to use when trying to establish a causal relationship between variables when the dependent variable is binary.

Other options to the Logistic Model are the Probit and Linear Probability Models. Since there are very small differences between probit and logistic regressions, logistic regressions with results reported as odds ratios was used, as guided by the literature (Singer, Weiser & McCoy 2014). Odds ratios was favoured to reporting marginal effects since it will ease comparison with earlier studies. The Linear Probability Model can be a good option and provide more easily interpreted outputs. However, as Wooldridge (2016) concludes, this model has certain

limitations and can end up reporting probabilities below zero or above one. Since the data used in this study is very skewed towards people being adherent to their treatment, the Linear Probability Model would be problematic to use.

3.3 Main variables

The outcome variable in this study is adherence and it has been measured through the Center for Adherence Support Evaluation (CASE) method of self-reported adherence. The advantages of using a self-reported adherence measure is that it is quick, inexpensive and interferes less with the personal integrity of the interviewee than for example unannounced pill counts. By collecting data on adherence through visits to respondents' homes instead of at clinics at the time of ARV refill, respondents with poor clinical attendance were still included, reducing the selection bias that could otherwise have occurred.

In accordance to the CASE method, people in the study who were currently on ART were asked three questions in order to establish their level of adherence. The questions had a set of possible answers that were read out to the person being interviewed by the nurse performing the interview (see appendix A2). From the answers, a CASE Adherence Index score was calculated, with a range from 3-16. People with a score >10 were classified as adherent and a score ≤10 as non-adherent, creating a binary variable with the value 0 for non-adherent and 1 for adherent[2]. Two participants reported taking ARV's even though they tested negative for HIV. These two observations were excluded from analysis, since it is unclear if this is a lab mistake or mistake in the collection of the survey data, leaving 2226 observations of PLHIV on ART out of the 10 236 respondents in the study.

The research hypothesis is that food insecurity will compromise adherence to ART. The opposite of food insecurity - food security is defined by the Food and Agriculture Organization as follows: "All people, at all times, have physical and economic access to sufficient, safe and nutritious food to meet their dietary needs and food preferences for an active healthy life" (Hendriks 2015). Identifying a measure of food security that considers all the aspects of food insecurity is difficult and as Hendriks et al. (2016) points out, no perfect measure exists. The measure used in this study is developed from questions used in the General Household Survey conducted in South Africa every year. The strength of this is that

[2] This method of measuring self-reported adherence was developed by the New York Academy of Medicine's (NYAM) Center for Adherence Support Evaluation (CASE). In a study where adherence was measured by both CASE Adherence Index and the older, more commonly used three-day self-report, the index was a better predictor of both the levels of viral load and CD4 counts (Mannheimer et al. 2006).

it allows for comparison with national data on food security as well as making replication of the study easier[3].

To calculate food insecurity, a set of eight questions were asked (see appendix A3) and a Food Adequacy Access Index (FAAI) score was calculated. One point was given for every affirmative answer, creating an index with a range from 0-8. 26 further observations were excluded at this stage since data on food insecurity was incomplete, reducing the number of observations included in the analysis to 2200.

3.4 Population and sample

The population in this study is defined as PLHIV in the two districts Vulindlela and Greater Edendale (see figure 2) of the uMgungundlovu Municipality in KwaZulu Natal that are currently on ART/have been on ART but stopped their treatment. The analysis is based on the sample of 2200 respondents that fulfilled the inclusion criteria discussed in the previous section.

3.5 Regression analysis with and without controlling for nutritional support

To investigate the relationship between food insecurity and adherence to ART, logistic regression where only the variable of interest was included was first run. This was done using STATA. Food insecurity was measured through dummies for each possible score in the FAAI to evaluate how different levels of food insecurity would affect adherence to ART. Results are reported at three significance levels; $p<0.10$, 0.05, 0.01.

In the study, 980 out of the 2200 included participants answered that they were currently receiving nutritional support. In the weighted dataset, this represented 45.5% of the HIV positive population on ART. This variable was interesting since it might have interactive effects with food insecurity: How would access to nutritional support affect the likelihood of adhering to treatment for people experiencing different levels of food insecurity? Before additional control variables were added to the regression model, the possibility of an interaction between these two variables was therefore tested.

[3] These questions are also recommended by Hendriks et al. (2016) in their study of different food security question-sets in South Africa (in the paper referred to as Stats SA's Complex Access to Food (CAF) Score).

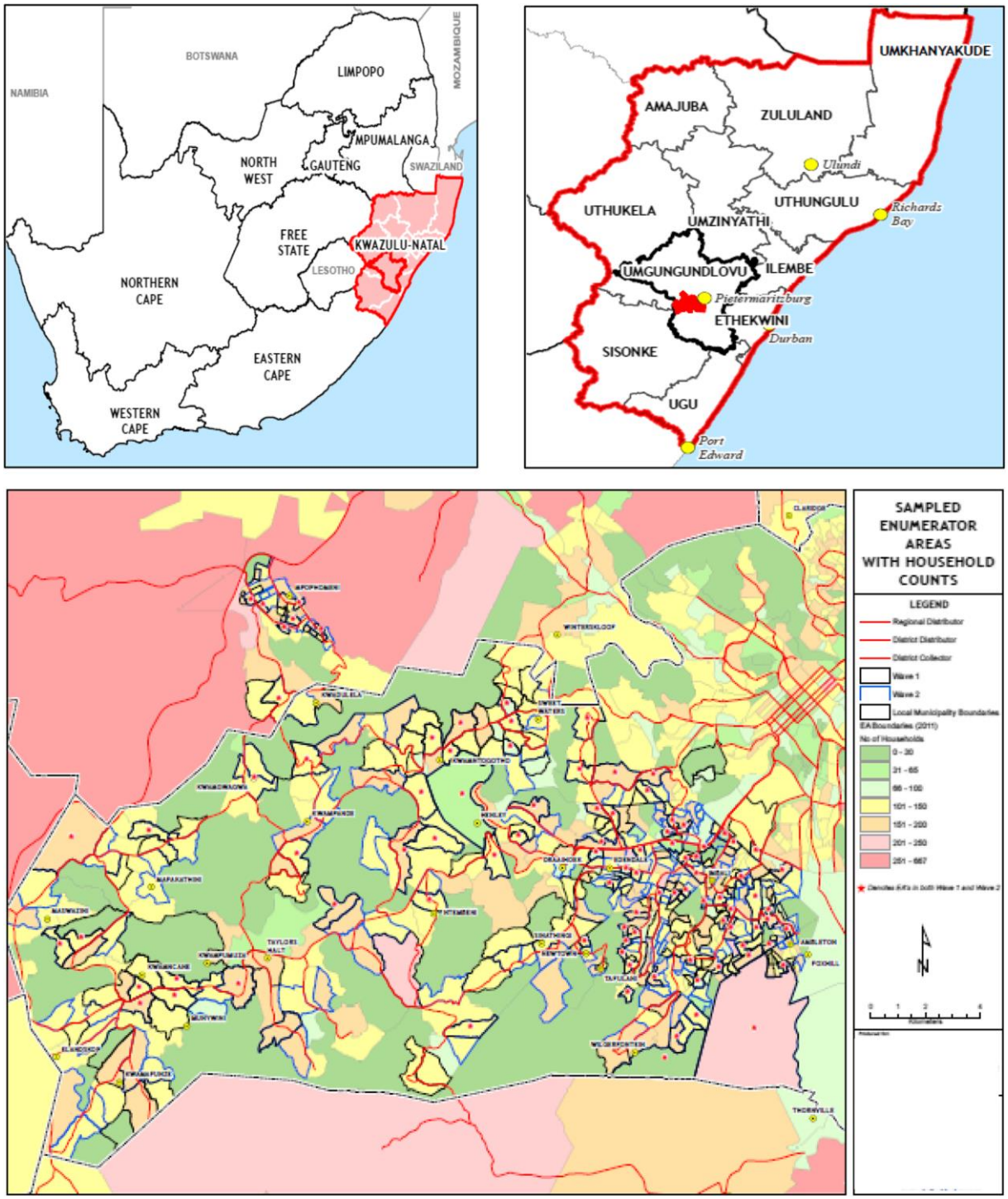


FIGURE 2. *Map of Greater Edendale and Vulindlela in KwaZulu Natal, South Africa (Kharzany et al. 2015, s. 4)*

Two additional ways of categorising food insecurity was applied at this stage, where the different scores on the FAAI was divided into categories. Firstly, utilising the categories defined by Statistics South Africa (Stats SA 2012) where households are divided into homes with: *adequate access to food* (a score of 0-1 on the FAAI), *inadequate access to food* (a score of 2-6) and *severely inadequate access to food* (a score of 7-8). Based upon the regression output from the unadjusted regression described previously, an alternative way of categorising the data seemed more relevant. Three categories were defined, with a slightly different cut-off: *food secure* (a score of 0-1 on the FAAI), *food insecure* (a score of 2-7) and *severely food insecure* (a score of 8).

A dummy variable, *nutritional support*, was created that assigned the value 1 if the respondent reported having access to nutritional support, and the value 0 if not. Three regressions were run; 1) Using dummy variables for each score on the FAAI and interaction terms created by taking the different scores*nutritional support. 2) Using dummy variables for the three categories *food secure, food insecure* and *severely food insecure* and corresponding interaction terms. 3) Using dummy variables for the three categories defined by Stats SA (explained above) and corresponding interaction terms. The last model is not included in the results section but can be found in appendix A5.

3.6 Multivariate regression analysis and control variables

Multivariate logistic regression with added control variables was lastly performed to reduce the risk of omitted variable bias. Control variables included in the regressions are described in table 1 and will also be discussed in this section.

Control variables chosen included demographic variables such as age, gender and marital status that are commonly controlled for. The variable age is divided into seven age categories instead of using one continuous variable, since the relationship between age and adherence might not be linear. All respondents reported being of "African" ethnicity and ethnicity/race was therefore not controlled for. Certain variables reflecting socioeconomic status, such as income level, was not included. Since ARV's are heavily subsidised and most people in the population were not paying for their medications, the income effect on adherence would be indirect, mediated through its effect upon for example food insecurity and ability to travel to the clinic. Therefore, the control variable *distance to the clinic* was included, but income level was not. The variable *income loss,* representing income loss suffered when going to the clinic instead of going to work was also included. Education was also controlled for in the model.

Apart from nutritional support, three further support functions were included in the study. These were financial support, treatment buddy and home care. Since these support functions could also influence adherence to ART they were included as controls. Emotional support was also reported, but not included due to high correlation with other support functions.

Alcohol consumption and especially alcohol abuse was important to control for, since it has repeatedly been found to be a barrier to treatment adherence (Shubber et al. 2016) and since we did not know if it might be positively correlated with higher degrees of food insecurity. Another relevant variable in this aspect was drug use. Participants were asked questions about multiple types of drugs, but only usage of two; qoh (ecstasy) and dagga was reported by participants. On the question whether respondents used any other drugs, some reported tobacco use. However, since this was not a question about tobacco there is a risk that other participants would not identify tobacco as a drug, and therefore not have reported it. This variable was therefore not included in the analysis even though tobacco use otherwise could have been relevant to control for.

Lastly, a control variable for depressive symptoms was included. To construct this variable a shortened version of the Center for Epidemiologic Studies Depression Scale (CES-D) was utilised (see appendix A4). A previous study of interest found that food insecurity often would lead to depression and it also found depression to be clearly linked to poor adherence (Whittle et al. 2016). Depression would according to this study be seen as a mediator through which food insecurity affects adherence to ART. In such a case, depression should not be controlled for in the regressions since it would lead to an estimated effect of food insecurity that is not as strong its true value. An additional regression was therefore run without this variable (see appendix A6).

TABLE 1. CONTROL VARIABLES

Type/name	Description
Access to support functions - Nutritional_support - Financial_support - Treatment_buddy - Home_care	Nutritional support was also included as interaction terms with food insecurity as described in the text. These are dummy variables that take the value 1 for people with access to the support function and 0 for respondents without access to the support.
Treatment regimen - Multiple_dose	Dummy variable that takes the value 1 for people on a multiple dose regimen (and 0 for people on a single dose regimen).
Gender - Male	Dummy variable that takes the value 1 for a man (and 0 if the respondent is a woman).
Age group - 20-24 - 35-39 - 25-29 - 40-44 - 30-34 - 45-49	Age of respondent (15-49 years) divided into 7 categories. Dummy variables were crated for each category, the age span 15-19 representing the benchmark category in regression analysis'.
Marital status - Marital_status_1 - Marital_status_2	Respondents answers divided into three groups: single people who had previously not lived with a partner (1), people who were legally married and/or lived with their partner (2) and respondents who had previously lived with a partner but for different reasons did not do so anymore. Three dummy variables were created with the third group mentioned being the benchmark group.
Highest finished level of education - Primary - Secondary - Incomplete_secondary - Secondary - Tertiary	Divided up into five dummy variables reflecting highest level of education: no schooling at all (benchmark group, not included), completed primary school, incomplete secondary school, completed secondary school and tertiary school.
Alcohol consumption - Using_alcohol - Bingedrinking	Using_alcohol takes the value 1 for respondents who drink alcohol (0 otherwise). Bingedrinking takes the value 1 for respondents that fulfil the definition of binge drinking as drinking 5 or more alcoholic drinks on the same occasion on at least 1 day in the past 30 days.
Using drugs - Drugs	Respondents reported usage of two types of drugs: dagga and qoh/ecstacy. If a respondent reported using either or of these drugs the dummy variable took the value 1, otherwise 0. Tobacco is not included.
Depressive symptoms - Depression	Variable based on a shortened version of the Center for Epidemiologic Studies Depression Scale (CES-D) (see appendix A4). A set of 5 questions were asked, respondents scoring on a scale from 0-15. [4]
Income loss from going to clinic - Income_loss	Dummy variable that takes the value 1 when a respondent reported that going to the clinic resulted in an income loss (0 otherwise).
Distance to clinic - 1-2_hours_to_clinic - 2-3_hours_to_clinic - >3_hours_to_clinic	Four dummy variables reflecting distance to clinic where ARV's are collected: less than one hour (benchmark group, not included), 1-2 hours, 2-3 hours, >3 hours.

[4] Additional regression is run in appendix A4, table 7, where a cut-off level of 4 for depressive symptoms is used, based on recommendations of Shrout and Yager (1989). A regression output where depression is not included among the control variables is also included in appendix A6 for comparison.

3.7 Endogeneity and missing data

There is a risk that important variables that are not included in this multivariate regression analysis exists, resulting in an issue with endogeneity. One example of a possible control variable that did not have reliable enough data to be included in the model was tobacco use. There is also a possibility that there exist other unobserved variables relevant to the model, leading to omitted variable bias.

Another piece of information that is not available in the collected data is how long respondents had been on HIV treatment. If treatment was started recently, then it could be easier to achieve a high score on the CASE Index, leading to overestimated levels of adherence. However, as long as food insecurity is not over- or underrepresented among people who started their treatment more recently, this is not considered to be a significant issue.

3.8 Connection to viral load suppression

Adherence is important in achieving viral load suppression. To test that our measure of adherence is a significant predictor of viral load, chi-square tests were used to evaluate the relationship between self-reported adherence and viral load. Viral loads were classified as undetectable when <50 copies/ml blood, supressed when <1000 copies/ml blood and un-supressed when ≥1000 copies/ml blood.

3.9 Descriptive statistics

In this section, an overview of the population characteristics will be given and firstly, the high rates of HIV infection are worth mentioning; The estimated HIV prevalence in the study area was 35,2% (diagram 1). This is a lot higher than the countrywide estimates from 2015 of 19.2% HIV prevalence in this age group (UNAIDS 2016b).

Out of the HIV positive population, an estimated 55.3% were on treatment and 1.3% had been on ARV's but reported having quit their treatment. The remaining 43.3% of PLHIV were not and had not received treatment. Also worth mentioning is that HIV prevalence was significantly higher among women than men. This can be observed in diagram 2 where the proportion of HIV positive women and the proportion of HIV positive men in the population are reported separately.

DIAGRAM 1.

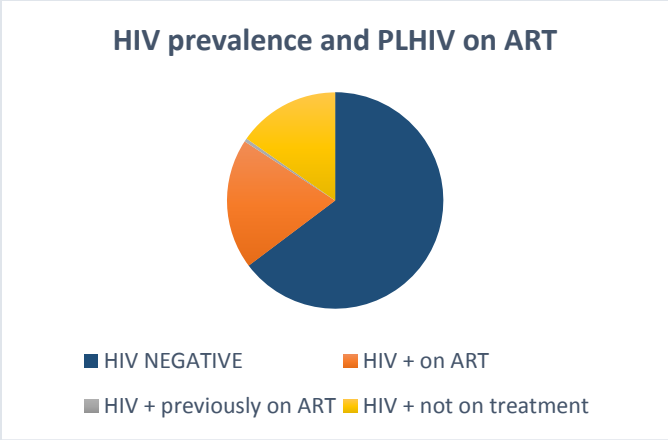
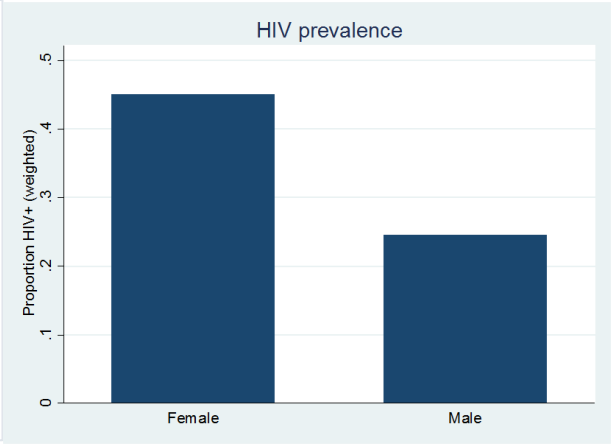
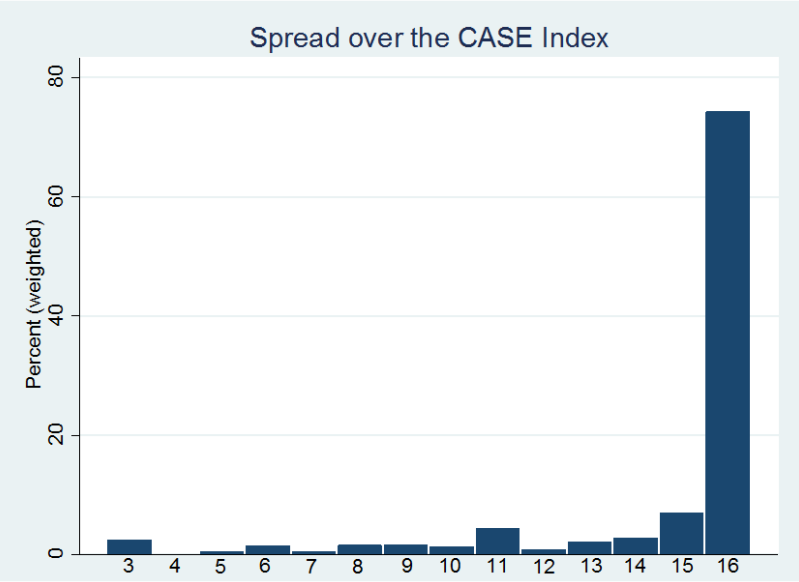


DIAGRAM 2.



The outcome variable in following analysis' is adherence to ART and the level of adherence to treatment according to the CASE Index was found to be high. This is illustrated both in diagram 3 and through summary statistics in table 2. 91.1% of people on ART were reportedly adherent to their treatment regimens (scoring >10 on the CASE Index). The 8.9% non-adherent (scoring ≤10 on the CASE Index) included respondents that had quit their treatment completely.

DIAGRAM 3.

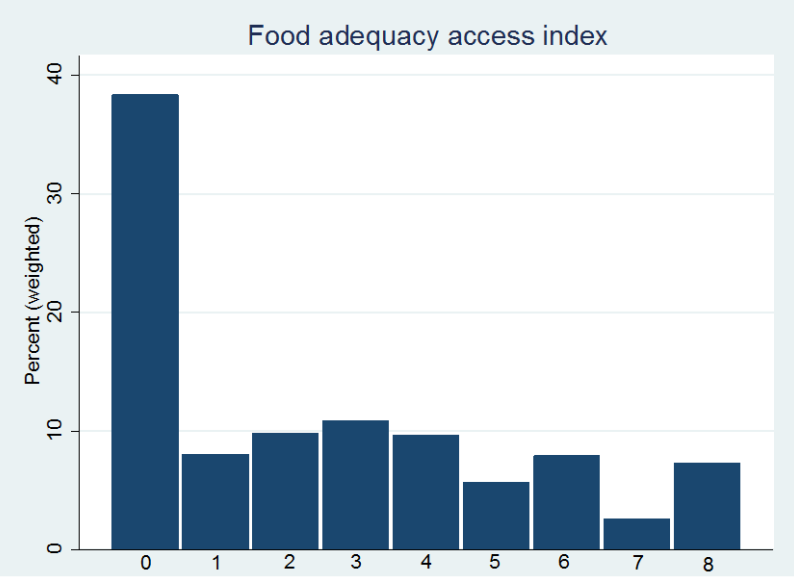


There is a risk that the level of adherence described in the previous paragraph could be overestimated and that participants reported higher levels of adherence than is really the case, due to social desirability bias; the tendency for participants to want to report the socially desired answer to a question (van de Mortel 2008). As can be seen in diagram 3, a high

percentage of participants (74,2%) reported that they had never missed taking a tablet and never missed taking it on time, giving them the highest CASE score of 16. This number appears high. However, grouping the observations into adherent and non-adherent decreases the risk of overestimated adherence levels since it's likely that respondents with a score of 16 would have a score of at least 11 even if the highest possible score is an overestimation. Further, there is no reason to believe that there would be a systematic difference in misreporting between food secure and food insecure respondents. This means that an overestimation of adherence levels will only lead to attenuation bias when evaluating a possible relationship between food insecurity and adherence.

The independent variable of interest, food insecurity was described by the Food Adequacy Access Index and as illustrated in diagram 4, a big proportion of households reported not having adequate access to food. Only some estimated 46,4% of households where respondents would test positive for HIV and report being/having been on ART would have adequate access to food (scoring 0 or 1 on the FAAI). The most severely food insecure (scoring 8 on the FAAI) represented 7.3% of the population.

DIAGRAM 4.



When dividing food security into the three categories: *food secure* (FAAI 0-1), *food insecure* (FAAI 2-7) and *severely food insecure* (FAAI 8) the data on adherence and food insecurity was combined. As illustrated in diagram 5, adherence rates are high in all categories. Even among people suffering from the highest degree of food insecurity, most of the population managed to adhere to ART.

DIAGRAM 5.

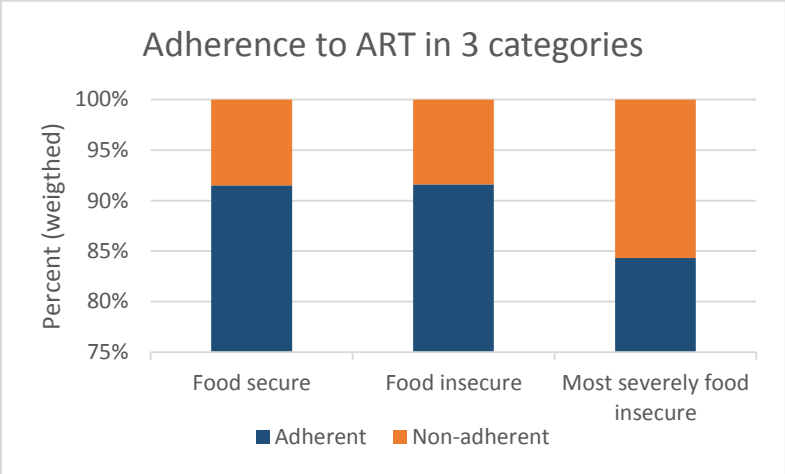


Table 2 below contains summary statistics of main variables and control variables. The control variable *depression* is a discrete variable. Remaining variables are binary and the mean here represents the estimated proportion of the population that falls into each of these categories. *Adherent to treatment* is the outcome variable, which has been discussed above. *Food insecure* and *severely food insecure* represents the variable of interest, also discussed above.

TABLE 2. SUMMARY STATISTICS

Variable	Mean	Std. Dev	Min	Max
Adherent to treatment	0.910	0.008	0	1
Food insecure	0.463	0.018	0	1
Severely food insecure	0.073	0.007	0	1
FI*nutr.support	0.214	0.016	0	1
SFI*nutr.support	0.040	0.005	0	1
Nutritional support	0.455	0.022	0	1
Financial support	0.062	0.008	0	1
Treatment buddy	0.316	0.020	0	1
Home care	0.239	0.018	0	1
Multiple dose	0.121	0.009	0	1
Male	0.296	0.012	0	1
Age 20-24	0.053	0.005	0	1
25-29	0.148	0.008	0	1
30-24	0.210	0.010	0	1
35-39	0.250	0.011	0	1
40-44	0.183	0.010	0	1
45-49	0.128	0.009	0	1
Marital status 1	0.704	0.013	0	1
Marital status 2	0.240	0.012	0	1
Primary schooling	0.078	0.007	0	1
Incomplete secondary schooling	0.549	0.015	0	1

Secondary schooling	0.329	0.014	0	1
Tertiary schooling	0.033	0.005	0	1
Using alcohol	0.267	0.012	0	1
Binge drinking	0.093	0.009	0	1
Drugs	0.015	0.003	0	1
Depression	3.518	0.117	0	15
Income loss	0.081	0.008	0	1
1-2 hours to clinic	0.259	0.014	0	1
2-3 hours to clinic	0.019	0.004	0	1
> 3 hours to clinic	0.013	0.003	0	1

Weighted summary statistics based on the sample of 2200 PLHIV included in the analysis.

4. Results & Discussion

In this chapter results from the study are presented and discussed. Firstly, the high adherence rates found in the study are discussed. After that, the results from regression analysis' are presented and nutritional support discussed. Lastly, the relationship between adherence and viral load is briefly analysed and discussed.

4.1 Adherence rates

The adherence rates to antiretroviral therapy of 91.1% found in this study indicates that the health care delivery for PLHIV in this high prevalence area has been successful. People that receive ART seem to be ready for treatment, manage well to adhere and have access to the support that they need. However, as Van Dyk (2010) points out, studies reporting high levels of adherence should be interpreted with caution. In a study on adherence to ART in South Africa published in 2010, Van Dyk found that as few as 40% of respondents managed to reach optimum adherence levels. In a meta-analysis, conducted by Mills et al. (2006b) consisting of 27 studies from 12 sub-Saharan countries, it was found that 77% of the study populations managed to adhere to treatment. Why are the adherence rates found in this study significantly higher? One explanation could be the several support initiatives existing in the study areas. An estimated 65.1% of PLHIV on ART was receiving treatment support at the time of the study. This took the form of either nutritional or emotional support, treatment buddy, home based care or financial support. Such programs and initiatives might contribute to the promising data on adherence, however as seen further down in the adjusted regression analysis (table 6) only receiving home care has a significantly positive effect on adherence in this analysis. With an odds ratio of 1.76 the odds of adhering to treatment is noticeably higher among PLHIV with access to home care ($p<0.1$ level). Nutritional support has a significantly positive effect on adherence when included as an interaction term with food insecurity, however this positive effect on adherence is only seen among the severely food insecure.

Another explanation for improved adherence rates in comparison to earlier studies could be improvement in treatment regimens. An estimated 87.9% of PLHIV on ART were on fixed/single dose treatment regimens. Compared to the pill burden for PLHIV on ART in South Africa a few years ago, this represents a big change and can be compared to the 1.1% of participants who had access to single dose regimens in an adherence study performed by Van Dyk in 2010. Since difficult treatment regimens have been found to be an important hindrance to adherence (Orrell et al. 2003, Mills et al. 2006a), this could be another explanation for the high adherence rates found in this study. As seen in the adjusted regression analysis (table 6), being on a multiple dose regimen instead of a single dose regimen lowers the odds of adhering to treatment to almost half (O.R.=0.58, $p<0.05$).

Limitations in the study that could have affected the reported adherence levels are the lack of data on when treatment was started for respondents and social desirability bias. Data on how long a respondent had been on ART was not available in this study and therefore all participants on treatment irrespective of start date were included in the analysis. If such data had been available and a restriction to people who had been on treatment for example > 6 months had been possible, this could have affected the results. As discussed in the previous chapter, there is also a risk that these estimates are subject to social desirability bias.

4.2 Regression analysis

In the first regressions run, it was tested whether a relationship existed between food insecurity and adherence to treatment when not including control variables. Results are presented in table 3.

Even though the model in table 3 not is significant, the results suggest that the severest level of food insecurity has a negative influence on adherence. The odds ratio of 0.51 suggests that the odds of being adherent in this group is half that of the odds of being adherent in the benchmark group where respondents suffered no food insecurity. A score between 1 and 7 on the FAAI does however not seem to have any relevant effect upon the probability of adhering to treatment in this study.

TABLE 3. REGRESSION ANALYSIS

Simple model:	**Probability of being adherent to ART**	
Variable	O.R. [95%CI]	P-value
FAAI score of 1	1.06 [0.52-2.18]	0.862
FAAI score of 2	0.92 [0.48-1.79]	0.813
FAAI score of 3	0.93 [0.45-1.92]	0.835
FAAI score of 4	1.05 [0.53-2.10]	0.882

FAAI score of 5	1.17 [0.50-2.74]	0.718
FAAI score of 6	1.12 [0.56-2.23]	0.750
FAAI score of 7	1.57 [0.39-6.23]	0.523
FAAI score of 8	0.51 [0.28-0.94]	0.032**
cons	10.59 [7.44-15.07]]	0.000***
Prob > F		0.547

Benchmark group was the part of the population with a FAAI score of 0. Prob > F=model significance. **Statistically significant at p<0.1, **p<0.05, ***p<0.01.*

4.3 Controlling for nutritional support

In the following step, the regression model was extended to control for nutritional support, to see how this would affect the results. An estimated 45.5% of the population studied was receiving nutritional support of some kind. When controlling for nutritional support and adding interaction terms into the model, results indicated (p<0.10) that having access to some sort of nutritional support increased the odds of adhering to treatment three times for people suffering from the highest level of food insecurity. In table 4 this is illustrated by the odds ratio for the interaction term *FAAI score of 8*nutritional support*. The effect on adherence of suffering from the highest level of food insecurity was highlighted when controlling for this interaction. In the group with the highest FAAI score and no nutritional support the odds of adhering to treatment was only one third of the odds in the food secure, benchmark group (O.R.=0.30, p<0.01).

TABLE 4. REGRESSION ANALYSIS, CONTROLLING FOR NUTRITIONAL SUPPORT (1)

Model adjusted for nutritional support:	**Probability of being adherent to ART**	
Variable	O.R. [95%CI]	P-value
FAAI score of 1	0.99 [0.39-2.53]	0.989
FAAI score of 2	0.71 [0.32-1.61]	0.415
FAAI score of 3	1.12 [0.32-3.89]	0.856
FAAI score of 4	1.06 [0.43-2.66]	0.894
FAAI score of 5	0.72 [0.23-2.22]	0.561
FAAI score of 6	1.01 [0.39-2.58]	0.991
FAAI score of 7	0.66 [0.16-2.82]	0.575
FAAI score of 8	0.30 [0.14-0.65]	0.002***
FAAI score of 1*nutritional support	1.13 [0.30-4.27]	0.852
FAAI score of 2*nutritional support	1.83 [0.51-6.48]	0.350
FAAI score of 3*nutritional support	0.69 [0.15-3.12]	0.630
FAAI score of 4*nutritional support	1.04 [0.30-3.66]	0.947
FAAI score of 5*nutritional support	3.25 [0.57-18-44]	0.182
FAAI score of 6*nutritional support	1.24 [0.31-4.91]	0.756
FAAI score of 7*nutritional support	1 (omitted due to perfect prediction)	
FAAI score of 8*nutritional support	3.02 [0.85-10.73]	0.087*
Nutritional support	0.75 [0.41-1.35]	0.334
cons	12.15 [7.90-18.67]	0.000***
Prob > F		0.520

Interaction terms with nutritional support added for each FAAI score. Benchmark group=the subpopulation with FAAI scores of 0. Prob>F=model significance.**Statistically significant at p<0.1 **p<0.05 ***p<0.01*

Since the access to food only appears to have an effect for the severely food insecure in this study, regression analysis was also run with food insecurity divided into three categories. When food insecurity was divided into these groups (described in the data section), the effect of being in the severely food insecure group is significant at the p<0.01 level (see table 5). We also see that the odds of adhering to treatment seem to significantly increase in this group when having access to nutritional support (O.R.=2.96, p<0.10), which was also observed in the previous model.

TABLE 5. REGRESSION ANALYSIS, CONTROLLING FOR NUTRITIONAL SUPPORT (2)

Model adjusted for nutritional support:	**Probability of being adherent to ART**	
Variable	O.R. [95%CI]	P-value
Food insecure	0.89 [0.51-1.57]	0.692
Severely food insecure	0.30 [0.14-0.63]	0.002***
FI*nutr.support	1.34 [0.60-2.97]	0.469
SFI*nutr.support	2.96 [0.85-10.37]	0.089*
Nutritional support	0.76 [0.44-1.32]	0.331
cons	12.13 [8.28-17.78]	0.000***
Prob > F		0.050**

Food insecurity is in this regression divided into the three categories *food secure*, *food insecure* and *severely food insecure*. Benchmark group was the part of the population defined as food secure. FI*nutr.support/SFI*nutr.support = interaction terms between *Food insecure/Severely food insecure* and *nutritional support*. Prob > F=model significance. **Statistically significant at p<0.1, **p<0.05, ***p<0.01*.

The findings described in the paragraphs above suggests that nutritional programs have a positive effect on adherence for PLHIV living in the most vulnerable households. This is in line with arguments that can be made based on described theory. Nutritional support would reduce reported side-effects from taking medicines without proper nourishment, and could also reduce uncertainty about the day-to-day life. This would allow people to plan for the future by investing more in future health, in this case by taking their ARV's and showing up to clinical visits.

Previous literature on the subject and the human behaviour of hyperbolic discounting, introduced in the theory chapter, provides arguments for why and how a lack of food would act as a hindrance to adherence to ART. A negative correlation between food insecurity and adherence was therefore expected. The size of such a correlation was however not conjectured and the so-called sign effect was mentioned as a possible mitigating factor of hyperbolic behaviour. In the regression analysis' presented, the hypothesized correlation is observed and statistically significant. The findings are also highlighted when including access to nutritional

support into the model. (For regression output with cut-off points in accordance with the Stats SA classification, see appendix A5).

The fact that a significant negative relationship between food insecurity and adherence is only observed for the highest possible score on the FAAI raises questions. Why is not the same relationship seen for people scoring 7 on the FAAI? - A score that also reflects a household with severe lack of food. And how do these findings relate to earlier research findings? With only 24 observations of people scoring 7 on the FAAI, the fact that we can't see a relationship between the two variables at this level might be due to a lack of power. Further, it is not the first time that a significant relationship between poor adherence and food insecurity is only found among respondents from households classified as severely food insecure. In a study in Namibia, Hong et al. (2014) found that respondents suffering from severe food insecurity were significantly more likely to adhere poorly to ART (O.R.=3.84, 95% CI 1.65 to 8.95). Even though different methods were used to determine both food insecurity and adherence rates, limiting comparability, these findings are similar to those of this study.

4.4 Regression analysis, including controls

Multivariate logistic regression with additional control variables was in the next step run (presented in table 5). This showed that even when controlling for various omitted variables, the odds of being adherent were lower among people living in severely food insecure households (see table 6). According to the model described in table 6, the odds of adhering to treatment among the severely food insecure and without access to nutritional support would be less than half of the odds among the food secure (O.R.=0.42, $p<0.05$). The significant results found for the interaction term *SFI*nutr.support* in the model described in table 5 has now disappeared.

Other variables that were significantly related to lower odds of adhering to treatment included: depression ($p<0.001$), alcohol consumption, drug use and being on a multiple dose regimen ($p<0.05$), having completed studies on a secondary level and having 2-3 hours travel distance to the clinic ($p<0.1$). Having access to home care increased the odds of adhering to treatment ($p<0.1$). Even though the results for having depressive symptoms were highly significant, the odds ratio of 0.93 only indicates a small decrease in the odds of being adherent. Having completed secondary school lowered the odds of adhering considerably in comparison to having no schooling at all (O.R.=0.15) is surprising. However, this should be interpreted with caution since it is only significant at the $p<0.1$ level.

Importantly, the odds ratio only compares the odds of adhering in one group to the odds of adhering in the benchmark group. Even though the odds of adhering to treatment among the severely food insecure are less than half of the odds of adhering in the food secure category, most people are in fact adherent to treatment in both categories. This is owing to the high adherence rates found in the study.

TABLE 6. MULTIVARIATE REGRESSION ANALYSIS

Adjusted model:	**Probability of being adherent to ART**	
Variable	O.R. [95%CI]	P-value
Food insecure	0.97 [0.52-1.08]	0.915
Severely food insecure	0.42 [0.19-0.90]	0.027**
FI*nutr.support	1.27 [0.54-3.00]	0.581
SFI*nutr.support	2.51 [0.71-8.92]	0.154
Nutritional support	0.78 [0.43-1.42]	0.409
Financial support	0.51 [0.22-1.21]	0.125
Treatment buddy	0.87 [0.53-1.41]	0.564
Home care	1.76 [0.98-3.13]	0.057*
Multiple dose	0.58 [0.35-0.95]	0.032**
Male	0.86 [0.54-1.37]	0.527
Age 20-24	0.45 [0.14-1.44]	0.180
25-29	0.92 [0.32-2.73]	0.890
30-34	1.04 [0.37-2.92]	0.945
35-39	1.18 [0.39-3.54]	0.766
40-44	0.90 [0.32-2.49]	0.838
45-49	1.02 [0.34-3.08]	0.974
Marital status 1	1.08 [0.53-2.20]	0.823
Marital status 2	1.13 [0.52-2.44]	0.759
Primary schooling	0.18 [0.02-1.66]	0.129
Incomplete secondary schooling	0.17 [0.02-1.47]	0.106
Secondary schooling	0.15 [0.02-1.37]	0.092*
Tertiary schooling	0.40 [0.03-5.44]	0.492
Using alcohol	0.51 [0.30-0.87]	0.013**
Binge drinking	0.72 [0.39-1.32]	0.283
Drugs	0.39 [0.16-0.95]	0.037**
Depression	0.93 [0.87-0.98]	0.009***
Income loss	0.56 [0.33-0.96]	0.035**
1-2 hours to clinic	1.01 [0.66-1.56]	0.963
2-3 hours to clinic	0.44 [0.17-1.16]	0.096*
> 3 hours to clinic	0.40 [0.11-1.39]	0.148
cons	143.69 [11.86-1740.82]	0.000***
Prob > F		0.000***

Prob > F=model significance. **Statistically significant at p<0.1, **p<0.05, ***p<0.01.*

4.5 Nutritional support

Even though the significant results found for the interaction term *SFI*nutr.support* disappeared in multivariate analysis, earlier results indicated an effect on adherence. Understanding what kind of nutritional support is available in the community is therefore of

relevance. To get a better insight into the subject, visits to clinics and one of the schools in the study area were conducted. Additionally, a search online for information on feeding schemes in the area was done. Emails were sent and phone calls were made to relevant organisations. Information gathered about nutritional support offered from clinics, feeding schemes in schools and food support from other organisations in the area will briefly be discussed in the following paragraphs.

Clinics in KwaZulu Natal offer nutritional support to underweight patients if they fill specific requirements. In the age group 15-49 year olds, this will, according to interviews[5] and guidelines (KwaZulu Natal Department of Health 2013), mainly be given to patients that suffer from HIV or tuberculosis. However, claiming that one does not have enough food to take ones ARV's is not enough to fulfil requirements, as the nutritional advisor at one of the clinics pointed out[6]. For those who do meet the requirements, a monthly food supply is given consisting of: 1) Enriched Maize Meal Porridge 2) Ready-to-Use Therapeutic Food (RUTF), a fortified peanut butter 3) Energy Drinks. The patient will then be monitored monthly in hope to see a healthy weight gain. This sort of nutritional support is given for up to six months, but can in some cases be extended[7] (KwaZulu Natal Department of Health 2013). Problems discovered with this nutritional support function was 1) Deliveries were not always reliable. At one of the clinics it was reported that the last delivery of food parcels had been months ago and the nutritional advisor only had one parcel left to hand out. 2) Even though all clinics should have a nutritional advisor that works specifically with issues of weight and nutrition, this is not always the case. This was seen at one of the clinics visited. They still gave nutritional support to patients at the clinic however.

Nutritional support could also come from the schools for the part of the population that was still attending secondary school. Both primary and secondary schools in poorer areas are subject to the National School Nutrition Programme (NSNP). This is a government funded programme that applies to schools in the study area and it assures that pupils in these schools get one nutritious meal every school day (Department of Basic Education 2014)[8]. The weekly

[5] Head nurse at Snathing Clinic & Nutritional Advisor at Grange Clinic, interviews on the 15th of February 2017.
[6] Nutritional Advisor at Grange Clinic, interview on the 15th of February 2017.
[7] Nutritional Advisor at Grange Clinic, interview on the 15th of February 2017.
[8] In the study population, 106 out of 1 557 participants that responded to a question about unemployment reasons gave "Full-time studies" as a reason. However, only slightly under 50% of these respondents reported having access to nutritional support, either not considering the NSNP or not having access to the NSNP (for example 13 of these participants that studied at a tertiary level).

menu from one of the schools[9] in the area is given in appendix A7 as a sample menu of such meals. In the school visited it was reported that this was working well. However, problems with inconsistent food delivery and lack of gas for heating up food are issues that could exist.

Other organisations that work with nutritional support does exist in the area and the Community Chest is spending 366 000 ZAR in their 2016/17 budget on improving food security in the area (Pietermaritzburg Community Chest 2017). Their biggest partner is an organisation called Stop Hunger Now. However, this collaboration started only in august 2016 and was not in place when the data for this study was collected. None of their nutritional support programs are targeted specifically at PLHIV, several are targeted at children and youth that is not a part of the studied population in this thesis[10]. Other help organisations in the area working with food aid include Project Gateway and the Pietermaritzburg Benevolent Society. However, it appears as if the majority of nutritional support at the time of the study would have been received through clinics and schools and was not specifically targeted at PLHIV.

4.6 Correlation with viral load

To test the relationship between adherence and viral load in the blood, chi-square analysis was used. Adherence was significantly correlated with viral load in the blood (Pearson uncorrected chi2(2) = 101.7117, F=38.7862, P = 0.000). 91,8% of adherent respondents were estimated to have supressed viral loads and 83,5% would have undetectable levels of virus in their blood. This can be compared to the corresponding values of 69,4% and 59,4% for those who are non-adherent. Even though these results are significantly different from each other, further analysis suggests that this correlation is not very strong (corr=-0.22). This could for example be because all people on ARV's are included in the analysis', irrespective of how long they have been on treatment – something that would affect viral load.

5. Conclusions

This thesis has investigated the relationship between food insecurity and adherence to antiretroviral therapy, a relationship that is increasingly recognized and examined in different settings. Below the main conclusions from the study are summarized.

Although high adherence rates are found, this study indicates that adherence is negatively influenced by food insecurity for the most vulnerable members of the society, people suffering from severe food insecurity. No indications are found that people suffering from a

[9] Mpande High School in KwaMpande, The Msunduzi Rural

[10] Zane Mchunu, Project Manager at Pietermaritzburg Community Chest, phone call on the 6th of march 2017.

milder degree of food insecurity will be less likely to achieve a high level of adherence to their medication. This study therefore identifies the most vulnerable parts of the society as a key population where food insecurity will influence adherence to ART. Indications are also given that food supplement programs can increase adherence for PLHIV in this category, even though significance is lost when controlling for other variables. This would mean that food supplement programs such as nutritional support from clinics and feeding schemes in schools have a positive effect on adherence to ART. However, this would have to be studied further to draw conclusions on the topic. Even though adherence rates are lower among people suffering from severe food insecurity, it should be mentioned that this was not found to be an absolute hindrance to adherence. However, assisting the economically vulnerable by reducing severe food insecurity could positively affect adherence and help ensure the attainment of the UNAIDS 90-90-90 goals.

The study has several limitations. The fact that the independent variable is measured at a household level instead of an individual level is problematic. The study assumption was that the reported level of food insecurity in the household was also representative for the individual interviewed in that household. However, food might be split unequally between members of the family. For example, in a family where someone has HIV and is in need of food, that individual might be prioritized when food split between family members. If that would be the case in many households, then the effect of food insecurity on adherence might be underestimated in this study. If this was the case, it could also be an explanation as to why significant results are only found for PLHIV in the most vulnerable families. This remains only speculation. A further issue with the measure of food insecurity is that it measures self-perceived hunger. Different people in the same situation might answer differently even though they are in comparable situations, which could also affect the data. No available data on how long respondents had been on ART limited the analysis and working with self-reported data, there is the risk of respondents reporting higher levels of adherence than is the case. Homeless people and people living in shelters was not included in the study since the study was conducted by random sampling of houses in the study area. This causes a selection bias where the most marginalised members of the community are not included. Finally, using cross-sectional data also limits our possibilities to draw conclusions about causality.

As mentioned in the paragraph above, there are reasons to analyse the reportedly high levels of adherence in this study with caution. However, it is not the first time high levels of adherence are reported in this area. Previous studies on adherence to ART in KwaZulu Natal

by both Ncama et al. (2008) and Peltzer et al. (2010) found adherence levels above 80%. Since then, one of the improvements in ART is that treatment regimens have become simpler through the introduction of single dose regimens. As difficult treatment regimens have been found to be an important hindrance to adherence (Orrell et al. 2003, Mills et al. 2006a), this could be one explanation for the high adherence rates observed in this study. Further research in the uMgungundlovu District would be interesting to try to understand the key determinants for achieving high rates of adherence.

Food security remains not only relevant for adherence but also contributes to better health outcomes. Even though further research might be necessary to verify the relationship found in this study, the fact that virologic suppression is aided by proper nutrition (Kalichman et al. 2015) provides further evidence of the importance of food security among PLHIV.

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Appendix

A1

Data collection

The data used in this essay comes from a big cohort study as explained in the data section. In this cohort, 10 236 individuals aged 15-49 years were randomly selected through a process described by Kharsany et al. (2015). People were eligible if they were in the right age-span, provided written informed consent in English or Zulu and were willing to take part in all the study procedures, which included clinical testing for both HIV and other sexually transmitted diseases and tuberculosis when indicated. Parental consent was also needed if the participant was < 18 years of age.

The study staff consisted of trained nurses with training in how to collect the data. Interviews were performed in the participants' homes and upon arrival to a randomly selected household appropriate introductions were made and the head of the household/designee identified. A household composition form was then completed in order to establish the age, gender, and basic socio-demographic profile of all household members. Here questions on food insecurity were asked, which therefore reflects food insecurity on a household level. Study staff collected the data through a handheld personal digital assistant (PDA) which, upon completion of the composition form, randomly selected one individual who met the eligibility criteria to be asked if they were willing to participate in the study. There was in other words a two-step randomization process, where first the household and then the individual where randomly selected. In cases where the selected individual chose not to participate, the PDA chose a new randomly selected person from the household. Upon a second refusal, the household was replaced.

Upon consent from a participant, he/she was assigned a unique study number. This was linked to a questionnaire with structured questions that were read out to the participant by the nurse and answers were filled in directly in the PDA, reducing risks of error by being programmed to go to the right follow-up questions and having set answer options. Interviews were conducted as private as possible, away from other family members. Questions covered a range of topics, including demographic, psycho-social and behavioural variables as well as HIV status variables. Upon completion of the questionnaire and taking of clinical samples a small

token in the form of a hat and a pair of gloves. Was given to the participant. Apart from that, no payment was made for participation.

To further strengthen the reliability of the results, a Quality Control team did random checks to see that data collected was correct and answers were also audited throughout the period of data collection and interview location and length of visit automatically registered by the PDA.

A2

Case Adherence Index questionnaire

A1. How often do you feel that you have difficulty taking your HIV medications on time? By 'on time' we mean no more than two hours before or two hours after the time your doctor told you to take it.

4 Never
3 Rarely
2 Most of the time
1 All of the time

A2. On average, how many days per week would you say that you missed at least one dose of your HIV medications?

1 Everyday
2 4–6 days/week
3 2–3 days/week
4 Once a week
5 Less than once a week
6 Never

A3. When was the last time you missed at least one dose of you HIV medications?

1 Within the past week
2 1–2 weeks ago
3 3–4 weeks ago
4 Between 1 and 3 months ago
5 More than 3 months ago
6 Never

The CASE Index score is calculated by adding up the points received on each of the three questions above. A score between one and four is possible on the first question and a score between one and six on the following questions. Index range: 3-16

Classification:

A score >10 = good adherence A score ≤10 = poor adherence

A3

General Household Survey Questions on Food Security

A1. Did your household run out of money to buy food during the past year?

Expects a single option response (**required**)

- ☐ **Yes** [1]
- ☐ **No** [2]
- ☐ **Did not respond** [98]

A2. Has it happened 5 or more days in the past 30 days? *(Skipped if A1 ≠ yes)*

Expects a single option response (**required**)

- ☐ **Yes** [1]
- ☐ **No** [2]
- ☐ **Did not respond** [98]

A3. Did you cut the size of meals during the past year because there was not enough food in the house?

Expects a single option response (**required**)

- ☐ **Yes** [1]
- ☐ **No** [2]
- ☐ **Did not respond** [98]

A4. Has it happened 5 or more days in the past 30 days? *(Skipped if A3 ≠ yes)*

Expects a single option response (**required**)

- ☐ **Yes** [1]
- ☐ **No** [2]
- ☐ **Did not respond** [98]

A5. Did you skip any meals during the past year because there was not enough food in the house?

Expects a single option response (**required**)

- ☐ **Yes** [1]
- ☐ **No** [2]
- ☐ **Did not respond** [98]

A6. Has it happened 5 or more days in the past 30 days? *(Skipped if A5 ≠ yes)*

Expects a single option response (**required**)

☐ **Yes** [1]

☐ **No** [2]

☐ **Did not respond** [98]

A7. Did you eat a smaller variety of foods during the past year than you would have like to, because there was not enough food in the house?

Expects a single option response (**required**)

☐ **Yes** [1]

☐ **No** [2]

☐ **Did not respond** [98]

A8. Has it happened 5 or more days in the past 30 days? *(Skipped if A7 ≠ yes)*

Expects a single option response (**required**)

☐ **Yes** [1]

☐ **No** [2]

☐ **Did not respond** [98]

Food Adequacy Access Index is calculated by giving one point for every affirmative answer. Range: 0-8. People who did not respond to the questions were excluded from analysis.

Categorization 1:

0-1	Adequate access to food
2-6	Inadequate access to food
7-8	Severely inadequate access to food

Categorization 2:

0-1	Food secure
2-7	Food insecure
8	Severely food insecure

A4

Shortened version of CES-D used in the study

Instruction: We would like you to describe ways that you may have felt or behaved during the last week.

A1. I felt depressed.

Expects a single option response (**required**)

- ☐ Rarely (Less than 1 day) [1]
- ☐ Some of the time (1-2 days) [2]
- ☐ Occasionally (3-4 days) [3]
- ☐ All of the time (5-7 days) [4]

A2. My sleep was restless.

Expects a single option response (**required**)

- ☐ Rarely (Less than 1 day) [1]
- ☐ Some of the time (1-2 days) [2]
- ☐ Occasionally (3-4 days) [3]
- ☐ All of the time (5-7 days) [4]

A3. I had crying spells.

Expects a single option response (**required**)

- ☐ Rarely (Less than 1 day) [1]
- ☐ Some of the time (1-2 days) [2]
- ☐ Occasionally (3-4 days) [3]
- ☐ All of the time (5-7 days) [4]

A4. I felt lonely.

Expects a single option response (**required**)

- ☐ Rarely (Less than 1 day) [1]
- ☐ Some of the time (1-2 days) [2]
- ☐ Occasionally (3-4 days) [3]
- ☐ All of the time (5-7 days) [4]

A5. I could not get going.

Expects a single option response (**required**)

- ☐ Rarely (Less than 1 day) [1]
- ☐ Some of the time (1-2 days) [2]
- ☐ Occasionally (3-4 days) [3]
- ☐ All of the time (5-7 days) [4]

Answers gave a shortened version of the **Center for Epidemiologic Studies Depression Scale.** Each question gave a score between 0-3. 0, for the answer "Rarely" and 3 for the answer "All of the time". Range: 0-15.

Regression with depression scale cut-off level of 4

This shortened version of the CES-D was developed based on the findings of Shrout and Yager (1989). In a large study, they found that a shortened 5-item version of the CES-D scale was nearly as sensitive and specific as the full 20-item scale, suggesting that such a scale could be used to save resources. In the analyses in this thesis, a cut-off level is not used. Shrout and Yager suggests that the original cut-off of 16 can be multiplied by n/20 when using a shortened scale (n= number of questions in shortened version). For a robustness check, the multivariate regression analysis is run with this cut-off level. This does not change the significance level for any of the results except the depression variable itself that is now significant at the p<0.05 level with an odds ratio of 0.58. Including a depression with this cut-off only slightly changes odds ratios the confidence intervals, while significance remains. This is displayed in the shortened regression output in table 7 below.

TABLE 7. MULTIVARIATE REGRESSION ANALYSIS

Adjusted model:	**Probability of being adherent to ART**	
Variable	O.R. [95%CI]	P-value
Food insecure	0.98 [0.52-1.84]	0.944
Severely food insecure	0.40 [0.18-0.87]	0.020**
cons	134.76 [11.27-1610.75]	0.000***
Prob > F		0.000***

In this regression analysis control variables include all control variables included in the multivariate analysis displayed in table 6, only changing the variable depression. Results are significant at the same significance levels as found in table 6 for all variables but depression. Prob > F=model significance.
**Statistically significant at p<0.1, **p<0.05, ***p<0.01.*

A5

TABLE 8. REGRESSION ANALYSIS

Model adjusted for nutritional support:	**Probability of being adherent to ART**	
Variable	O.R. [95%CI]	P-value
Inadequate access to food	0.91 [0.52-1.60]	0.741
Severely inadequate access to food	0.36 [0.18-0.73]	0.004***
Inad*nutr.support	1.23 [0.56-2.72]	0.604
Severely.inad*nutr.support	3.31 [0.98-11.18]	0.053*
Nutritional support	0.76 [0.44-1.32]	0.331
cons	12.13 [8.28-17.78]	0.000***
Prob > F		0.105

Food insecurity is in this regression divided into the three categories defined by Stats SA. Benchmark group was the part of the population defined as having adequate access to food. Inad*nutr.support/ Severely.inad*nutr.support = interaction terms between *Inadequate access to food/ Severely inadequate access to food* and *nutritional support*. Prob > F=model significance. **Statistically significant at p<0.1, **p<0.05, ***p<0.01.*

A6

TABLE 9. MULTIVARIATE REGRESSION ANALYSIS

Adjusted model:	**Probability of being adherent to ART**	
Variable	O.R. [95%CI]	P-value
Food insecure	0.92 [0.50-1.69]	0.793
Severely food insecure	0.37 [0.17-0.79]	0.010***
FI*nutr.support	1.23 [0.52-2.88]	0.634
SFI*nutr.support	2.46 [0.69-8.69]	0.163
Nutritional support	0.81 [0.44-1.50]	0.498
Financial support	0.47 [0.20-1.08]	0.073*
Treatment buddy	0.87 [0.53-1.44]	0.593
Home care	1.72 [0.98-3.03]	0.061*
Multiple dose	0.57 [0.35-0.92]	0.023**
Male	0.89 [0.56-1.43]	0.642
Age 20-24	0.47 [0.15-1.50]	0.204
25-29	0.87 [0.30-2.52]	0.799
30-34	1.03 [0.37-2.87]	0.954
35-39	1.16 [0.39-3.43]	0.786
40-44	0.89 [0.33-2.44]	0.823
45-49	0.98 [0.33-2.95]	0.973
Marital status 1	1.03 [0.51-2.08]	0.926
Marital status 2	1.08 [0.50-2.35]	0.833
Primary schooling	0.20 [0.02-1.75]	0.143
Incomplete secondary schooling	0.19 [0.02-1.57]	0.122
Secondary schooling	0.17 [0.02-1.47]	0.107
Tertiary schooling	0.45 [0.03-5.76]	0.534
Using alcohol	0.51 [0.30-0.86]	0.012**
Binge drinking	0.68 [0.38-1.22]	0.194
Drugs	0.37 [0.16-0.89]	0.026**
Income loss	0.55 [0.32-0.94]	0.029**
1-2 hours to clinic	1.01 [0.66-1.55]	0.966
2-3 hours to clinic	0.45 [0.18-1.15]	0.095*
> 3 hours to clinic	0.39 [0.10-1.46]	0.160
cons	103.26 [9.15-1165.03]	0.000***
Prob > F		0.000***

Prob > F=model significance. **Statistically significant at p<0.1, **p<0.05, ***p<0.01.*

A7

Weekly food menu in one of the schools in the study area, as part of the National School Nutrition Programme:

Monday – Putu, chicken and butternut

Tuesday – Rise, tinned fish, carrot and tomatoes

Wednesday – Rice, soya and potatoes

Thursday – Samp, sugar beans and cabbage

Friday – Rice, soya, potatoes and carrots

Meals were served at 10.00 every day.