

Measure of adherence to antiretroviral treatment amongst HIV positive patients attending antiretroviral clinics in selected rural, deep-rural and semi-urban areas of Ugu District in KwaZulu-Natal

Phumelele Perseverence Mthethwa

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PREFACE

This study was undertaken to measure adherence levels of patients taking antiretroviral treatment in rural, deep rural and semi-urban areas, to compare the factors that affect adherence in these areas, and to establish whether the geographical location of the facilities has an impact on the level of adherence to treatment.

DECLARATION

I, Mrs Phumelele Perseverence Mthethwa declare that:

- (i) The work described in this dissertation has not been previously submitted to UKZN or any other tertiary institution for purposes of obtaining a degree or any other academic qualification, whether by myself or any other party
- (ii) The research reported in this dissertation, except where otherwise indicated, is my original work. Together with my supervisor I conceptualised the topic, I developed the protocol and the ethics application with the guidance and support of my supervisor and statistician, conducted the survey and entered the data by myself and together with the statistician and guidance by my supervisor, completed the analysis of the data obtained.
- (iii) I drafted the article and together with my supervisor's guidance, input and support submitted the article to the journal. I have completed the dissertation with the guidance and support of my supervisor.
- (iv) This dissertation does not contain another person's data, graphs, tables or other information, unless specifically acknowledged as being sourced from other persons.
- (v) This dissertation does not contain other person's writing, unless specifically acknowledged as being sourced from other researchers. Where other written sources have been quoted, the information used has been referenced accordingly.



Signed: _____

Date: 30 November 2017

Name: Phumelele Perseverence Mthethwa

Name: Dr. Panjasaram Naidoo

Supervisor

DEDICATION

To my husband, my children, my parents and my brother:

Thank you for the love, guidance, motivation and support throughout my academic career.

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LIST OF ACRONYMS AND DEFINITIONS

Adherence: Adherence to long term therapy is defined as the extent to which a person's behaviour (taking medication, following a diet and/or executing lifestyle changes) corresponds with the agreed upon recommendations from a health care provider.

AIDS: Acquired Immune Deficiency Syndrome

ARV: Antiretroviral

ART: Antiretroviral Therapy

FDC: Fixed dose combination

HAST: HIV/AIDS, STI & TB

HIV: Human Immunodeficiency Virus

KZN: KwaZulu-Natal

Rural area: Any area that is not classified as urban. Rural areas are subdivided into tribal areas and commercial farms.

Deep-rural area: an area that is not classified as urban and usually under jurisdiction of tribal authorities, headed by chiefs, while sub-chiefs are direct principals of villages. These areas are generally with limited general basic services such as water and sanitation facilities.

Semi-urban area: an area between a rural and an urban area, or partially urban, that which is not wholly characteristic of an urban area.

STI: Sexually transmitted infections

TB: Tuberculosis

WHO: World Health Organization

ABSTRACT

Background

The roll-out of antiretroviral (ARV) treatment in public health facilities was initiated in 2004 in the KwaZulu-Natal province. The roll-out made ARV treatment available and accessible to the vast majority of the population which previously could not afford treatment due to their low socio-economic status. Adherence levels need to be monitored timeously in order to ensure that patients are adherent to their treatment. Treatment outcomes are affected by the level of adherence to treatment. Adherence to treatment is essential in providing a sustainable and effective antiretroviral rollout campaign. The ARV roll-out has been initiated in all areas of society in South Africa, and it is a known fact that there are certain factors that affect the level of adherence. It is therefore critical to measure the level of adherence to treatment by patients and to assess the factors that affect adherence. Few studies were done to determine whether geographical location of the patients and their clinics had an effect on adherence. This study was therefore undertaken with the following aims and objectives

Aim and Objectives

The specific objective of the study was to describe the demographics of the patients attending ART clinics in rural, deep rural and semi-urban areas of Ugu District in KwaZulu-Natal, to measure the level of adherence to ARV therapy, and to determine the factors that affect adherence to the therapy in these areas.

Method

A retrospective chart analysis of 1020 Human Immunodeficiency Virus (HIV) infected patients (18-60 years of age) who reside in Ugu District within the catchment population of the facility, registered on the ART programme in the facility and have been receiving ART from the facility for at least 2 years were selected to be in the study. The following research sites were chosen: 1 rural hospital, 1 deep-rural clinic and 1 semi-urban community health centre was chosen. Records of the patients from January 2011 to December 2014 were examined in order to select the patients. A closed-ended, coded questionnaire was administered to all patients in the study & was used to record the demographics, level of adherence and factors affecting adherence. After obtaining their consent the questionnaires were administered. The data was captured and analysed using SPSS version 23 software.

Results

Of the 1020 patients, there were 623 females (61%), with most patients between 18-35 years (56.9%). Almost 70% of the patients were African, with 57.5% single and 75.9% having less than 3 dependants. Forty nine percent of the patients had secondary level education, whilst 61.2% of them

were unemployed. More than 62% of the patients use public transport to get to these facilities. Over two thirds of the patients (67%) were on the Fixed Dose Combination treatment, with 70% of the patients already on treatment for 2-4 years, and 30% on treatment for more than 4 years. More than half of the patients (51.7%) had missed between 2-4 appointments to collect their medication from health facilities in the previous 6 months. Although 80.9% of the respondents indicated that they understood the importance of adherence ($p=0.008$) an overall 58.5% were actually adherent to treatment, with the majority coming from the deep rural area ($p=0.001$).

A number of factors affected the adherence to treatment for patients in the 3 areas, both positively and negatively, the first being their transport to the facility. A larger percentage of patients in the deep-rural (12.4%) area reported taking 2-3 hours ($p=0.000$) to arrive at these facilities due to transport problems. Over ten percent in the deep-rural area reported having travelled 15-20km ($p=0.00$). The second reason related to weather, where a much larger proportion of patients (73.8%) in the deep-rural area associated the weather with their ability to reach the health facilities to collect their medication. Other reasons included waiting time, where a great majority of patients from the semi-urban area (87.1%) reported to having waited longer than 2 hours to be attended to. With respect to stock outages 15.4% of patients in all 3 areas were affected by stock outages. Over 40% (42.8%) of the overall patients were affected by family deaths. They could not attend their clinics resulting from having to make arrangements for the burial of their loved ones. This significantly affected patients in the deep rural area (54.4%). Close to 25% of patients were the only caregivers at home, thereby sometimes being unable to collect their medication from the facilities due to having small dependants who cannot be left unattended at home. A greater majority (75.9%) of patients admitted to not collecting their medication from health facilities due to having sufficient treatment at home, with the smaller proportion (66.8%) being in the rural area ($p=0.00$). Forty two percent of patients related being depressed as one of the reasons for not taking their medication, with the larger proportion (49.4%) being in the semi-urban area ($p=0.004$). Over half of all patients (50.7%) used traditional medicines with the reported use of alcohol higher in the deep-rural area (93.5%) than in the other areas. Just over a quarter of the participants were involved in substance abuse. A larger proportion (62.4%) of patients who did not disclose their status were in the semi-urban area, compared to the other 2 areas ($p=0.008$), with 69.8% of patients indicating a fear of loss of social grant if adherent to treatment. This fear was much greater in the deep-rural area (88.5%) than in the other areas ($p=0.000$). A larger proportion of patients (30.9%) in the semi-urban area reported that they were not granted leave from work to collect their medication. Regimen changes affected adherence in 32% of patients while compliance to treatment for 67.9% of the patients was affected by side-effects. The association between mistrust of the new single tablet and adherence was statistically significant ($p=0.023$). A lower proportion of urban patients (35.6%) showed mistrust compared to the other areas, and 18.8% of patients taking single agents missed one of the two daily doses, with most (25.9%) of the patients

who missed the dose being from the semi-urban area. Over 51% of patients did not see the need of taking their medication due to feeling better. This generally affected all 3 areas.

Ninety two percent of patients in the deep-rural area indicated that they felt safe in the facility compared to the other areas. Just over half of the patients attending the semi-urban area clinic liked their facility, compared to 91.8% of the deep-rural area and 95.9% of the rural area patients. Staff attitude affected adherence, where 71.2% in the deep-rural area felt that the staff attitude was good compared to the perception of patients in the other two areas ($p=0.00$). A larger proportion (87%) of the patients in the semi-urban area reported food frequently being available thus enabling them to take their medication, whilst 46.5% of these patients felt that reminder methods were not effective compared to 57.4% (rural) and 58.5% (deep-rural).

Conclusion

The adherence levels of patients in rural, deep-rural and semi-urban areas are affected by various factors. The area of residence had statistical significance in some of the factors that affected adherence, while some factors were cross-cutting across all the areas of residence.

CHAPTER 1

1. Introduction

1.1 Background and Literature Review

South Africa has the biggest and most high profile HIV epidemic in the world, with an estimated 7.1 million people living with HIV in 2016. One third of all new infections in the region in 2016 were in one country: South Africa.¹ In the same year, there were 270,000 new infections while 110,000 South Africans died from AIDS-related illnesses.¹

South Africa has the largest antiretroviral treatment (ART) program globally and these efforts have been largely financed from its own domestic resources. The country now invests more than R22 billion annually to run its HIV and AIDS programmes.² However, HIV prevalence remains high (18.9%) among the general population, although it varies markedly between regions.¹ For example, HIV prevalence is almost 40% in KwaZulu-Natal compared with 18% in Northern Cape and Western Cape.³

Although more potent ARV regimens can allow for effective viral suppression at moderate levels of adherence,^{4, 5, 6} partial or non-adherence can lead to the development of resistant strains of the virus. Some of the common barriers identified and cited include fear of disclosure, alcohol use, traditional medicine use, feeling better on treatment, inadequate knowledge about the disease and ARVs, stigma, transport costs,^{7, 8, 9} lack of social support (financial and emotional), discrimination, depression and hopelessness, not being able to disclose their HIV status and a lack of food,⁹ service related factors,⁸ patients beliefs and behaviours,⁸ pill burden and drug side effects.⁸

Patients' behaviour is the critical link between a prescribed regimen and treatment outcomes. The most effective regimen will fail if the patient does not take the medication as prescribed or refuses to take it at all. Consequently all things being equal, the most important factors influencing adherence are patient-related.^{10, 11}

Adherence to long term therapy, according to WHO,¹⁰ is defined as a person's behaviour (taking medication, following a diet and/or executing lifestyle changes) corresponding with the agreed upon recommendations from a health care provider.

Poor adherence can lead to clinical, immunological and virological failure with the latter resulting into the spread of drug resistant forms of the virus which is of public health concern. It can also lead to increased costs to health and society as a result of direct financial costs of failed treatment and higher hospitalisation rates.¹²

Since the gold standard approach for assessing ART adherence has not been established many researchers use patient self-reporting because of its low cost and simplicity, although this measure has

led to underestimation of non-adherence. Pharmacy adherence measures (PAM) are also relatively simple to administer and have provided more clinically relevant results compared to self-reports.¹³

Adherence is a dynamic process that changes over time and predictors of non-adherence vary considerably and therefore no single factor has been consistently associated with non-adherence across all studies.¹⁴

There is a need to establish whether the desired levels of adherence can be achieved and maintained in different settings (rural, deep rural and semi-urban) where patients living with HIV/AIDS live, collect and administer their ARV treatment; and what the determinants of adherence to ARV treatment in such settings are.

This study therefore focussed on measuring adherence levels of patients taking ARV treatment in rural, deep rural and semi-urban areas and compared the different factors that affect adherence in these different areas of society thereby establishing whether the geographical location of the facilities has an impact on the level of adherence to treatment.

1.2 Core Research Problem and Clinical Significance

With the advent of ART, HIV/AIDS has become a chronic disease, therefore adherence to HIV medication is an extremely complicated process that includes drugs to provide the conditions for effective drug therapy. Some regimens require several doses of medication per day together with various requirements or restrictions on food intake.^{10, 11}

Good adherence is crucial for maximum clinical benefit from antiretroviral therapy. Therefore despite increasing access to antiretroviral drugs, the long-term success of treatment programs in resource limited settings requires establishing the optimum levels of adherence. Factors that make patients on ART fail to obtain good adherence have to be determined and addressed.

Therefore, the statement of the research problem for this study is:

What are the factors that affect adherence to antiretroviral therapy in HIV positive patients treated in rural, deep rural and semi-urban areas of Ugu District in KwaZulu-Natal, and how adherent to ARV therapy are patients attending ARV clinics in these 3 different settings in Ugu District in KwaZulu-Natal?

The hypothesis is, therefore, that HIV positive patients visiting rural, deep rural and semi-urban ARV clinics in Ugu District are adherent to their antiretroviral therapy.

The current public health arena is grappling with issues of treatment adherence for chronic diseases. Knowledge gained from this study about factors in the population associated with adherence and non-adherence to antiretroviral therapy by HIV positive patients will help in making recommendations

regarding the development of appropriate health education strategies to empower patients about the importance of adherence to ART.

The information will be used to develop guidelines and education materials that can be used in adherence counselling before patients are started on ART and during the follow-up periods after starting.

The findings will also contribute to the review of the HIV/AIDS treatment protocols and policies, related in-service education for medical personnel and review of health education programs for HIV positive patients so as to improve the clinical management of HIV/AIDS.

A research poster based on the results can also be developed for presentation in seminars, workshops and related conferences to empower health professionals on issues of adherence to ART.

1.2 Aim of the study

The study aimed at conducting a survey in order to determine the factors that affect adherence to antiretroviral therapy in HIV positive patients treated in rural, deep rural and semi-urban areas of KwaZulu-Natal, and find out how adherent to ARV therapy are patients attending ARV clinics in these 3 different settings in KwaZulu-Natal.

1.3 Specific Objectives Of The Study

The following were the specific objectives of the study:

- To describe the demographics of the patients visiting the ARV clinics.
- To evaluate the level of understanding of patients with regards to the meaning and importance of adherence.
- To determine the level of adherence of patients in the 3 different geographical locations.
- To determine the factors affecting adherence to ARV treatment in rural, deep rural and semi-urban areas.

1.4 Methodology

The research methodology outlines the logical process of the research and what processes and procedures are followed to answer the research question and achieve the research objectives.¹⁵

1.4.1 Research Context

According to Polit & Beck,¹⁶ a research context is defined as a specific place where data collection occurs. Three (rural, deep-rural and semi-urban) health facilities within Ugu District in KwaZulu-Natal will be selected as the research context. Facilities that were chosen were facilities that provide comprehensive HIV/AIDS services.

Ugu Health District is found in the lower South Coast of the Province of KZN. The neighbouring Districts are Ethekwini and Sisonke. The estimated population is 760 285. The district provides health service to the population using the Primary Health Care approach through the District Health System and this is done at all levels of care.

This district comprises of six local municipalities namely: Vulamehlo, Umdoni, Umzumbe, Hibiscus, Izingolweni and Umzwebantu. There are also three Emergency Medical Rescue Service bases and three Medico-Legal Mortuaries

There are three District Hospitals, one Regional Hospital, one Specialised Hospital, two Community Health Centres; 56 fixed clinics (including three Gateway clinics), and 15 Mobile Clinics with 216 visiting points in 84 wards. There are ten local authority clinics in the District.

1.4.2 Study Population

According to Polit & Beck,¹⁶ the study population is defined as the entire aggregation of cases in which the researcher is interested. The target population however, is defined as the total group of subjects about whom a researcher is interested and from whom results could reasonably be generated.

For this study, the target population was all adults (i.e. 18 to 60 years of age) male and female HIV positive patients on ART for more than two years in Ugu District.

Accessible population, according to Polit & Beck,¹⁶ is the aggregate of cases that conform to designated criteria and are available as subjects for a particular study. Burns & Grove¹⁷ define it as the portion of the target population to which the researcher has reasonable access.

For this study, the accessible population was all adult male and female HIV positive patients accessing ART from the chosen rural, deep-rural & semi-urban health facilities in Ugu District in KZN.

1.4.3 Inclusion Criteria

Eligibility criteria, according to Polit & Beck,¹⁶ is the criteria that designates the specific attributes of the target population by which people are selected for inclusion in a study.

The following inclusion criteria was used to identify the study population

- Adult male and female (18-60 years of age).
- Registered as an ARV patient at the chosen facilities.
- Receiving ART from the chosen facilities
- Been on ART in the chosen facilities for at least two years.
- Resides in Ugu District, within the catchment population area of that particular facility.

1.4.4 Exclusion criteria

- All patients <18 years of age.
- All patients who had not completed two years being on ARV therapy.
- All patients who do not reside in Ugu District.

1.4.5 Sample and sampling technique

A sample is a subset of the study population that is selected for a particular study and the members of the sample are the respondents. Sampling is defined by Burns & Grove ¹⁷ as the process for selecting a group of people, events, behaviour or other elements with which to conduct a study.

A sampling technique is the method used to select a sample from the study population.¹⁶ At the time of the study, a total of 47 643 patients were on ARV treatment from the 63 health facilities in Ugu District. Three health facilities were selected for this study i.e. one rural (Murchison Hospital), one deep-rural (Elim Clinic) and one semi-urban (Gamalakhe CHC) facility. These 3 facilities were chosen based on having the highest volume of HIV patients collecting treatment within the 3 different geographical areas at the time of the study. A total of 9786 patients collected ARV treatment in the rural (n= 2982), deep-rural (n=3284) and semi-urban (n=3520) areas. A retrospective chart analysis was done of HIV positive patients who visited the health facilities from January 2011 to December 2014. The charts were reviewed on Mondays, Wednesdays and Fridays during ARV clinic days at the 3 sites. The patients who refused to be part of the study were excluded. Charts with missing records were also excluded from the study.

A total 1630 patients met the inclusion criteria (450 in the rural area, 560 in the deep-rural area and 620 in the semi-urban area). These were patients between 18-60 years of age, were receiving ART from the selected facilities in Ugu District and had been on treatment for 2 years or longer.

These results were submitted to the Statistician for input and validation of sample size. The Statistician suggested that a total sample size of 1020 patients be randomly chosen with 340 patients chosen from each area.

The random sampling approach was used to select the 1020 patients from the 1630 that met the inclusion criteria in order to obtain a representative sample. The first, and thereafter every sixth patient was chosen to randomly select a total of 340 respondents from each area.

1.4.6 Data Collection

Some studies define adherence using a categorical definition as “no missed or reduced doses” during a given time period and other set the criterion for adherence as meeting minimum level of drug consumption at 95% or more, measured using pill counts.

With reference to this study, adherence was measured as self-reported adherence to ART by the HIV positive patient that was measured against the available counted pills at the time of the following monthly visit to the health facility, with the minimum acceptable drug consumption of 95% i.e. Pharmacy refill method was used to measure adherence in this study. Adherence rates from pharmacy refill records are determined by comparing the actual with expected refill dates or by identifying “medication gaps”, defined as periods during which the patient’s supply of medication is assumed to have been exhausted.¹⁸

According to Polit & Beck,¹⁶ structured data collection involves a fixed set of questions to be answered in a specified sequence and with pre-designated response options.

The use of a questionnaire is associated with advantages such as less cost, respondent anonymity, absence of interviewer bias, easy to administer and data yielded is easy to analyse. However, it has disadvantages including low response rates, the questions tend to have less depth especially if they are closed-ended questions and the respondent is unable to elaborate on the response or ask for clarification of the questions.¹⁷

The study used a structured data collection approach in the form of a questionnaire with closed-ended questions. In this study, a structured questionnaire was utilised so as to focus the research process and also be able to quantify the results of the study phenomenon.

Consent was obtained from the respondents for the administration of the questionnaire. The questionnaire was then administered to all the 1020 respondents in order to determine the level of understanding of the importance of adherence, the level of adherence to treatment and the factors that affected adherence in the 3 geographical areas. A separate, private room was used to complete the questionnaire.

Variables recorded for each HIV positive patient meeting the set criteria were as follows:

- a. Demographics
 - (i) Age
 - (ii) Gender
 - (iii) Marital status
 - (iv) Race
 - (v) Level of education
 - (vi) Number of dependants
 - (vii) Occupation
 - (viii) Treatment regimen
 - (ix) Mode of transport
 - (x) Duration on ARV Therapy

- (xi) Period medication not taken
- b. Measure of adherence: adherence / non-adherence
- c. Factors affecting adherence
 - (i) Understanding the importance of adherence to treatment
 - (ii) Facility issues
 - Transport to the facility
 - Distance to the facility
 - Safety of the facility
 - Facility preference
 - Staff attitudes
 - Waiting time
 - Stock outages
 - (iii) Social issues
 - Family death
 - No other caregiver at home
 - Sufficient stock
 - Depression resulting from taking the medication
 - Food availability
 - Reminder methods not effective
 - Traditional medicine use
 - Alcohol use
 - Substance abuse
 - Non-disclosure of status
 - Fear of Social Grant loss
 - (iv) Work issues
 - No leave granted at work
 - (v) Weather
 - (vi) Feeling better
 - (vii) Time of taking medication
 - (viii) Quantity of tablets taken (pill burden)
 - (ix) Treatment regimen changes
 - (x) Side effects
 - (xi) Missed doses
 - (xii) Mistrust of the new single tablet

1.4.7 Validity

Validity is an important concept and is of concern throughout the research process. It is important to the researcher during the research process and to those who read the study report as they provide a basis for making decisions as they consider using the findings in their practice.

According to Polit & Beck,¹⁶ validity is defined as the degree to which an instrument measures what it is supposed to measure.

Validity varies from one sample to another and from one situation to another; therefore, validity testing actually validates the use of an instrument for a specific group or purpose rather than the instrument itself.

In this study, the degree of face, content, internal and external validity of the instrument for the intended purpose and the context where the study is conducted were determined.

In this study, face validity was ensured by carefully selecting the items to be included in the questionnaire. These items reflect the concept of adherence to ART and the factors that affect it in HIV positive patients. It was also established by consulting the medical colleagues of the researcher and the study supervisor to make inputs.

To enhance content validity, the questionnaire was presented for review to the statistician and study supervisor to make inputs. This helped in refining questions for better meaning, clarity and conceptualisation.

To enhance internal and external validity, it was ensured that the accessible population is as much as possible similar in characteristics to the target population.

1.4.8 Data Analysis

According to Burns & Grove,¹⁷ data analysis is defined as a process that is conducted to reduce, organise and give meaning to the collected data.

Quantitative data management and analysis was done using SPSS version 23 software (Chicago, Illions, USA) program with the assistance of the statistician.

The variables of the respondents such as age, gender, marital status, source of income, educational level, HIV status disclosure to spouse/partner, alcohol use and adherence level will be used in the analysis of data to describe and make inference to the sample population.

Chi-Square test was used to assess the variables. A p-value of < 0.05 was considered statistically significant.

1.5 Dissertation structure

Chapter 1:

- Background and Literature Review
- Core research problem and clinical significance of the study
- Formulation of aims and specific objectives of the study
- Research Methodology

Chapter 2: - Presentation of manuscript entitled “Does the geographical location of HIV positive patients attending antiretroviral clinics in selected rural, deep-rural and semi-urban areas of Ugu District in KwaZulu-Natal affect adherence?” submitted to the South African Family Practice Journal. Article is presently under review.

- Chapter 3:*
- Discussion of findings
 - Limitations of the study
 - Conclusion and recommendations

CHAPTER 2

Does the geographical location of HIV positive patients attending antiretroviral clinics in selected rural, deep-rural and semi-urban areas of Ugu District in KwaZulu-Natal affect adherence?

Prepared according to the Instructions for Authors of SOUTH AFRICAN FAMILY PRACTICE JOURNAL

Publication status: under review

Adherence to antiretroviral (ARV) treatment is essential in order to improve treatment outcomes. Many factors influence adherence to ARV treatment. However, not many studies have surveyed the impact of geographical location of patients as a factor contributing to adherence. This study was therefore undertaken to assess the level of adherence, the impact of the geographical location of patients on adherence levels and to confirm other factors that affect adherence in these areas.

Title of study

Does the geographical location of HIV positive patients attending antiretroviral clinics in selected rural, deep-rural and semi-urban areas of Ugu District in KwaZulu-Natal affect adherence?

Authors

Mthethwa PP, B.Pharm (UKZN)

Affiliation:

Discipline of Pharmaceutical Sciences

School of Health Sciences

University of KwaZulu-Natal

Naidoo P, B.Pharm(UDW), MMedSci(UDW), PhD(UKZN)

Discipline of Pharmaceutical Sciences

School of Health Sciences

University of KwaZulu Natal

Corresponding Author: PP Mthethwa

Contact details:

Postal Address: P.O. Box 30360, Richards Bay, 3900

Fax: 0866135747

Cell: 0833148515

Email: phumelelen@yahoo.com

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Adherence, factors, rural, deep-rural, semi-urban

Conflict of interest:

The authors declare that they have no financial or personal relationships which may have inappropriately influenced the writing of this paper.

Abstract

Background

Adherence to antiretroviral (ARV) treatment is essential in order to improve treatment outcomes. Many factors influence adherence to ARV treatment. However, not many studies have surveyed the impact of geographical location of patients as a factor contributing to adherence. This study was therefore undertaken to assess the impact of the geographical location of patients on adherence levels and to confirm other factors that affect adherence in these areas.

Methods

Retrospective chart analysis of 1020 Human Immunodeficiency Virus (HIV) infected patients (age >18-60 years; treatment period ≥ 2 years) in one rural, one deep-rural and one semi-urban health facility were analysed to determine the level of adherence. The 1020 patients were chosen by selecting the first, and thereafter every sixth patient. Charts with missing records were excluded from the study. A questionnaire was then administered to these patients to confirm adherence levels and determine factors that affected adherence.

Results

Majority (61%) of the respondents were females. Though 80.9% of all respondents understood the importance of adherence only 58.5% were adherent to treatment, with 89.4% of these adherent patients residing in the deep rural area. Factors affecting adherence were cited by respondents from certain geographical areas more than others, such as transport, facility preference, staff attitude, waiting time, food availability, alcohol use and social grant. There were also common factors affecting adherence in these respondents across the 3 geographical areas such as distance, stock, depression and mistrust of new single [Fixed Dose Combination] tablet.

Conclusion

Factors, due to the geographical location of the respondents, did affect the adherence whilst there were many other factors that affected adherence irrespective of their geographical location.

South Africa has the highest number of HIV infected people worldwide with an estimated 5.6 million people living with HIV.¹ The challenge has shifted from access to adherence with increased access to antiretroviral therapy.^{2,3} Although more potent ARV regimens can allow for effective viral suppression at moderate levels of adherence,^{4,5,6} non or partial adherence can lead to the development of resistant strains of the virus.

Some of the common barriers identified and cited include fear of disclosure, alcohol use, traditional medicine use, feeling better on treatment, inadequate knowledge about the disease and ARVs, stigma, transport costs,^{7,8,9} lack of social support (financial and emotional), discrimination, depression and hopelessness, not being able to disclose their HIV status and a lack of food,⁹ service related factors,⁸ patients beliefs and behaviours,⁸ pill burden and drug side effects.⁸ Patients' behaviour is the critical link between a prescribed regimen and treatment outcomes. The most effective regimen will fail if the patient does not take the medication as prescribed or refuses to take it at all. Consequently all things being equal, the most important factors influencing adherence are patient-related.^{2,10}

Adherence to long term therapy, according to WHO,² is defined as a person's behaviour (taking medication, following a diet and/or executing lifestyle changes) coinciding with the agreed upon recommendations from a health care provider. Poor adherence can lead to clinical, immunological and virological failure with the latter resulting into the spread of drug resistant forms of the virus which is of public health concern. It can also lead to increased costs to health and society as a result of direct financial costs of failed treatment and higher hospitalisation rates.¹¹

There is a need to establish whether the desired levels of adherence can be achieved and maintained in different settings (rural, deep rural and semi-urban) where patients living with HIV/AIDS live, collect and administer their ARV treatment; and what the determinants of adherence to ARV treatment in such settings are. This study therefore focussed on measuring adherence levels of patients taking ARV treatment in rural, deep rural and semi-urban areas and compared the different factors that affect adherence in these different areas of society thereby establishing whether the geographical location of the facilities has an impact on the level of adherence to treatment.

Methods

A retrospective chart analysis of 1020 Human Immunodeficiency Virus (HIV) infected patients (18-60 years of age) who reside in Ugu District within the catchment population of the facility, registered on the ART programme in the facility and have been receiving ART from the facility for at least 2 years were selected to be in the study. Research sites chosen were 1 rural hospital, 1 deep rural clinic and 1 semi urban community health centre. Records of the patients from January 2011 to December 2014 were examined in order to select the patients. The first, and thereafter every sixth patient was chosen to randomly select patients. Patients who refused to be part of the study were excluded. Charts with missing records were also excluded from the study. A closed-ended, coded questionnaire was administered to all patients in the study & was used to record the demographics, level of adherence and factors affecting adherence. After obtaining patient consent the questionnaires were administered. Most studies set the criterion for adherence as meeting minimum level of drug consumption at 95% or more, measured using pill counts. With reference to this study, adherence was measured as self-reported adherence to ART by the HIV positive patient that was measured against the available counted pills at the time of the following monthly visit to the health facility, with the minimum acceptable drug consumption of 95% i.e. Pharmacy refill method was used to measure adherence in this study. Adherence rates from pharmacy refill records are determined by comparing the actual with expected refill dates or by identifying "medication gaps", defined as periods during which the patient's supply of medication is assumed to have been exhausted.¹²

Using this method to record and measure adherence is common among settings in which medication is provided and financed in a single location especially in a closed pharmacy system provided that the refills are measured at several points in time.

The data was captured and analysed using SPSS version 23 software. A p-value of < 0.05 was considered statistically significant. Gatekeepers permission was given by the KwaZulu Natal Department of Health Research and Development Committee with the study given full ethical approval from the Biomedical Research Ethics Committee of the University of KwaZulu Natal (BREC No : 399/14)

Results

Socio-demographics

The socio-demographic profile of the respondents is shown in *Table I* below.

Table I: Socio-demographic profile of the respondents (n=1020)

	Overall n (%)	Rural n (%)*	Deep Rural n (%)*	Semi Urban n (%)*
Age				
18-35 years	580 (56.9)	188 (55.3)	268 (78.8)	124 (36.5)
36-60 years	439 (43.1)	151 (44.7)	72 (21.2)	216 (63.5)
Gender				
Female	623 (61)	204 (60)	212 (62.4)	207 (60.9)
Male	397 (39)	136 (40)	128 (37.6)	133 (39.1)
Race				
African	709 (69.5)	244 (71.8)	235 (69.1)	230 (67.6)
Asian	157 (15.4)	48 (14.1)	52 (15.3)	57 (16.8)
White	81 (7.9)	25 (7.4)	27 (7.9)	29 (8.5)
Coloured	73 (7.2)	23 (6.8)	26 (7.6)	24 (7.1)
Marital status				
Single	587 (57.5)	202 (59.4)	196 (57.6)	189 (55.6)
Married	433 (42.5)	138 (40.6)	144 (42.4)	151 (44.4)
No. of dependants				
0-3	774 (75.9)	254 (74.4)	235 (69)	285 (83.8)
≥ 3	246 (24.1)	86 (25.6)	105 (31)	55 (16.2)
Level of education				
No education	50 (4.9)	15 (4.4)	25 (7.4)	10 (2.9)
Primary level	316 (31.0)	91 (26.8)	167 (49.1)	58 (17.1)
Secondary level	500 (49.0)	173 (50.9)	99 (29.1)	228 (67.1)
Tertiary level	154 (15.1)	61 (17.9)	49 (14.4)	44 (12.9)
Employment				
Unemployed	624 (61.2)	204 (60)	190 (55.9)	230 (67.6)
Employed	396 (38.8)	136 (40)	150 (44.1)	110 (32.4)
Mode of transport				
Foot	131 (12.8)	48 (14.1)	43 (12.6)	40 (11.8)
Public transport	642 (62.9)	214 (62.9)	215 (63.2)	213 (62.6)

Lift club	112 (11.0)	35 (10.3)	38 (11.2)	39 (11.5)
Private vehicle	135 (13.2)	43 (12.6)	44 (12.9)	48 (14.1)

*% = total number of affected respondents/ total number of respondents in that area x100

Majority of respondents were females and in the 18-35 age group. Of this age group over 78% were from the deep rural area. Over 60% were unemployed. Forty nine percent of the patients had secondary level education. More than 62% of the patients use public transport to get to these facilities.

ARV Treatment

Table II: ARV Treatment (n=1020)

	Overall n (%)	Rural n (%)*	Deep Rural n (%)*	Semi Urban n (%)*
Current regimen				
Single agents	275 (27)	90 (26.5)	92 (27.1)	93 (27.4)
Fixed Dose Combination (FDC)	683 (67)	231 (67.9)	227 (66.8)	225 (66.2)
Regimen 2	62 (6)	19 (5.6)	21 (6.2)	22 (6.1)
Period on treatment				
2-4 years	711 (70)	241 (70.9)	266 (78.2)	204 (60)
>4 years	308 (30)	98 (28.9)	74 (21.8)	136 (40)
No. of missed appointments (2-4)	527 (51.7)	180 (52.9)	237 (69.7)	110 (32.4)

*% = total number of affected respondents/ total number of respondents in that area x100

Over two thirds of the patients (67%) were on the Fixed Dose Combination treatment, with over 51.7% missing 2-4 appointments, the majority coming from the deep rural area.

Adherence

Table III: Measure of adherence and the understanding of the importance of adherence by the respondents (n=1020)

	Overall n (%)	Rural n (%)*	Deep Rural n (%)*	Semi Urban n (%)*	P-value
Adherent to treatment	597 (58.5)	180 (52.9)	304 (89.4)	113 (33.2)	p=0.001
Understand the importance of adherence	825 (80.9)	326 (95.9)	312 (91.8)	187 (55.0)	p=0.008

*% = total number of affected respondents/ total number of respondents in that area x100

It can be seen from Table III that even though 80.9% of the respondents indicated that they understood the importance of adherence an overall 58.5% were actually adherent to treatment, with the majority coming from the deep rural area.

Factors affecting adherence

The factors affecting adherence are listed in Table IV below.

Table IV: Factors affecting adherence of HIV positive patients in rural, deep rural and semi urban areas (n=1020).

	Overall n (%)	Rural n (%)*	Deep Rural n (%)*	Semi Urban n (%)*	P-value
Factors adversely affecting adherence					
Transport to facility (2-3 hours)	95 (9.3)	38 (11.2)	42 (12.4)	15 (4.4)	p=0.000
Distance to facility (15-20km)	72 (7.1)	21 (6.2)	36 (10.6)	15 (4.4)	p=0.000
Weather	468 (45.9)	185 (54.4)	251 (73.8)	32 (9.4)	p=0.000
Waiting time (>2hours)	635 (62.3)	231 (67.9)	108 (31.8)	296 (87.1)	p=0.000
Stock outages	157 (15.4)	49 (14.4)	53 (15.6)	55 (16.2)	p=0.810
Family death	437 (42.8)	147 (43.2)	185 (54.4)	105 (30.9)	p=0.000
No other caregiver at home	253 (24.8)	78 (31)	51 (15)	124 (36.5)	p=0.000
Sufficient stock at home	774 (75.9)	227 (66.8)	271 (79.7)	276 (81.2)	p=0.000
Feeling depressed	433 (42.5)	126 (37.1)	139 (40.9)	168 (49.4)	p=0.004
Traditional medicine use	517 (50.7)	175 (51.5)	169 (49.7)	173 (50.9)	p=0.980
Alcohol use	759 (74.4)	178 (52.4)	318 (93.5)	263 (77.4)	p=0.000
Substance abuse	259 (25.4)	85 (25)	83 (24.4)	91 (26.8)	p=0.764
Non-disclosure of status	576 (56.3)	190 (55.9)	173 (50.6)	212 (62.4)	p=0.008
Social grant	712 (69.8)	264 (77.6)	301 (88.5)	147 (43.2)	p=0.000
No leave granted from work	308 (30.2)	103(30.3)	100 (29.4)	105 (30.9)	p=0.000
Pill burden (>4 tablets)	675 (66.1)	216 (63.5)	227 (66.8)	232 (68.2)	p=0.514
Regimen change	326 (32)	106 (31.2)	96 (28.2)	124 (36.5)	p=0.066
Side effects	693 (67.9)	235 (69.1)	230 (67.6)	228 (67.1)	p=0.995
Mistrust of new single tablet	413 (40.5)	121 (35.6)	136 (40)	156 (45.9)	p=0.023
Missed doses	192 (18.8)	40 (11.8)	64 (18.8)	88 (25.9)	p=0.000
Time of taking medication	134 (13.1)	46 (13.5)	25 (7.4)	63 (18.5)	p=0.964
Feeling better	523 (51.3)	179 (52.6)	162 (47.6)	182 (53.5)	p=0.254
Factors promoting adherence					
Facility safety	876 (85.9)	294 (86.5)	313 (92.1)	269 (79.1)	p=0.000
Facility preference	825 (80.9)	326 (95.9)	312 (91.8)	187 (55.0)	p=0.000
Staff attitude	610 (59.8)	207 (60.9)	242 (71.2)	161 (47.4)	p=0.000
Food availability	592 (58)	100 (29.4)	196 (57.6)	296 (87)	p=0.000
Reminder methods	552 (54.1)	195 (57.4)	199 (58.5)	158 (46.5)	p=0.002

*% = total number of affected respondents/ total number of respondents in that area x100

Table V: Summary of areas of residence mostly affected by the factors (positively and negatively)

Factors promoting adherence		
Deep-rural Area	Rural Area	Semi-urban Area
Clean and safe facility	Facility preference	Food availability
Good staff attitude		
Use of reminder aids		
Factors adversely affecting adherence		
Deep-rural Area	Rural Area	Semi-urban Area
Transport	Traditional medicine use	Waiting time
Distance	Side Effects	Stock outages
Weather		Having no other caregiver at home
Family death		Having sufficient stock at home
Alcohol use		Feeling depressed
Fear of loss of social grant		Substance abuse
		Non-disclosure of HIV status
		Not being granted leave from work
		Pill burden
		Regimen change
		Mistrust of new single FDC tablet
		Missing one of the two daily doses for patients not on FDC
		Time of taking medication
		Feeling better

Discussion

The majority of respondents being females, and the prevalence of HIV in the 18-35 age group is consistent with the 2012 survey which found that HIV prevalence amongst South African women was nearly twice as high as men,¹³ and that rates of new infections among women aged 15-24 were more than four times greater than that of men of the same age.¹⁴

With respect to their understanding, although 80.9% of the respondents indicated that they understood the importance of adherence, an overall 58.5% were actually adherent to treatment, with the majority (89.4%) coming from the deep rural area ($p=0.001$) compared to the rural (52.9%) and semi urban (33.2%) areas. This raises concerns as all patients included in this study had been on treatment for more than 2 years and provision of HIV/AIDS education and counselling to the patients is continuously done at every encounter with the healthcare providers at the healthcare facilities. The practice of being adherent by these patients appears to be neglected even though they are knowledgeable about the importance. A further survey determining what they actually understand about adherence and its importance should be carried out to devise appropriate interventions to help the patients obtain optimal adherence to ART.

In terms of the factors that affect adherence to ARV treatment, the time of travelling between home and the facilities was significantly associated with the area of residence ($p=0.000$). A larger percentage of patients in the deep-rural and rural areas reported taking 2-3 hours to get to the facility having to travel a distance of 15 to

20km at a cost. In a study done in Botswana¹⁵ it was reported that the cost incurred through transport to visit ART clinics was a major obstacle that had a negative impact on optimal adherence to ART. This concurs with results found in this study where distance travelled to health facilities impacts on the transport costs thus adversely affecting adherence due to the burden of paying for transport to ART sites.

The weather was significantly associated with the level of adherence to treatment ($p=0.000$). A much higher proportion of the deep-rural area patients (73.8%) associated the weather with their ability to collect medication from the health facility. Rainy weather makes it difficult to travel to ART sites from the deep rural area as rivers that are crossed on foot are sometimes full. Great discomfort is also caused by sunny weather for patients who walk to these facilities.

In terms of relating waiting time and adherence, there was a significant association noted between waiting time and adherence ($p=0.000$). A total of 635 (62.3%) patients waited in the queue for 2 hours and longer, with a significantly higher number of patients from the semi-urban ($n=296$; 87.1%) area reported having waiting times of greater than 3 hours. A previous study found that patients who stayed in queues for a long time (4 hours or more) before being helped by service providers find it difficult to fulfil all appointments as they think about past experiences encountered at the health facility.¹⁶

The death of a family member showed to have a statistical significance on level of adherence ($p=0.000$) and meeting their appointments. A total of 437 patients mentioned that family deaths affect them and hinders them from collecting their medication, with the highest number affected from the deep rural ($n=185$; 54.4%) area. This is due to cultural beliefs where limited mobility is part of the signs of mourning, mostly affecting African females who are expected to gather in a room with the grieving mother of the deceased. This probably accounts for over half of the patients (51.7%) missing between 2-4 appointments, the majority coming from the deep rural area.

At the time of data collection for this study, all patients chosen for the study were issued with one month's supply of medication. The pharmacy refill date given to the patient ensures that patients collect their next supply in time while the patients have not run out of medication. Overall, 774 (75.9%) of patients in this study indicated that having sufficient stock at home allowed them not to collect their next supply. Having stock at home by the time of the next refill appointment meant respondents were not taking their medication accordingly hence denoting non-adherence.

A patient's mental wellbeing can greatly affect adherence as feeling depressed may influence whether or not the patients end up taking their medication as required.¹⁷ There was a significant association between patients who felt depressed and adherence ($p=0.004$) in this study.

Half of the patients ($n=517$; 50.7%) in this study confirmed using traditional medicines, across all 3 areas of residence. Although there was no statistical significance, the influence of traditional healers and religious leaders undermined the evidence-based medical community's efforts to initiate and retain patients on ART, with dire morbidity and mortality consequences. Even after ART literacy classes, traditional beliefs outweighed faith in the healthcare system. The promise of a short-term, "curative" traditional remedy was more attractive than lifelong ART. Furthermore, traditional healer services were perceived by patients to be more attentive and individualized than clinic care, creating competition that discouraged ART.¹⁸

Family members' poor understanding of HIV and its transmission routes leads to stigmatization at home.¹⁸ Even though patients accept their HIV diagnosis they are still afraid to disclose to family members and sexual partners their HIV status for fear of being blamed for one's HIV infection or threat of expulsion from the home.²² In this study, there was a statistical significance between non-disclosure of status and adherence ($p=0.008$). A larger proportion (62.4%) of patients who did not disclose their status was in the semi-urban area, which contributed to lower adherence levels seen in this area.

In South Africa, AIDS sickness is coupled with eligibility for disability grants, and patients are entitled to a state-funded monthly income because of their illness-related incapacity to work. However, widespread unemployment has meant that disability grants are an important and at times the only source of income, even if patients are well enough to work. When disability grants are tied to AIDS-related indicators, such as CD4 counts or viral load, non-adherence may become an attractive option for patients who fear losing their grant if their CD4 count were to increase.²³ There was an association found between the fear of loss of social grant and adherence to treatment ($p=0.000$). Seventy percent ($n=713$) of patients feared losing their grants if their CD4 cell count improved, with the greatest fear in the deep rural area (88.5%).

In this study 396 respondents were employed, with 308 (77.8%) having reported not being granted leave or time off from work to collect their medication. This impacts the patient's ability to collect medication from health facility during the working hours of the health facility. It was reported that costs incurred through lost wages to visit ART clinics were major obstacles to adherence, concurring with findings of a study done in Botswana.¹⁵

Across all three regions, of the 623 (67%) patients on FDC in this study, a total of 413 respondents (66.3%) showed mistrust of the single FDC tablet. There was a significant association between the mistrust of the new single (FDC) tablet and adherence level ($p=0.023$). Hence education on the benefits of the FDC needs to be revised in order to allay their fears and mistrust.

The level of cleanliness of the environment as well as the perceived security of the respondents while within the facilities where they felt safe were reasons cited by patients that encouraged them to visit their clinics. There was a significant association ($p=0.000$) between adherence and safety of the facility. Most of patients ($n=876$; 85.9%) felt safe in the health facility across all 3 areas which positively affected adherence. This may somehow be associated with facility preference. Facility preference was higher in the rural and deep rural areas thus positively influencing adherence to treatment in these areas.

Studies previously done showed that the absence of a good patient and healthcare provider relationship and the poor attitude of the healthcare team at health facilities can be a significant barrier to adherence.²⁵ In this study, staff attitude showed a significant association with adherence ($p=0.000$). Almost 60% of patients received good staff attitudes from healthcare workers in the 3 different facilities, the highest being in the deep-rural area ($n=242$; 71.2%). This concurs with the findings of this study which showed the highest percentage of adherent patients being in the deep-rural area.

Food insecurity may affect the regularity of ART doses, as some patients have reported taking their medication only when they have food available.²³ This impacts on adherence because ARV medication cannot be taken on an empty stomach. There was a significant association between food availability and area of residence ($p=0.000$). Patients in the semi-urban area reported having food frequently available at home ($n=296$; 87%), compared to those in the rural ($n=100$; 29.4%) and deep-rural ($n=196$; 57.6%), yet surprisingly had the least level of adherence to treatment (33.2%).

A study done by Abdulrahman et al.²⁶ found that having daily reminders was one of the most important aids to taking medication on schedule. Taking medication on time positively affects adherence. In this study, there was statistical significance found between use of reminder methods and adherence levels ($p=0.002$). This affected patients equally in all the 3 different areas of residence.

Limitations

The largely rural location of the study may not be representative of the HIV-infected patient population at large. The study used a structured questionnaire which limited the possibility of in-depth understanding of the phenomenon under study since there were fixed responses to the questions that could not allow probing questions. With a survey, the accuracy of responses to the questions by respondents may be affected by recall bias. Adherence to long term therapy and its determinants is not a single incident but a continuous process over a period of time thus respondents may not be able to recall accurately their medication taking history.

Conclusion and Recommendations

More than half of the patients were adherent to treatment with the largest percentage residing in the deep-rural area, followed by rural then semi-urban area. Most factors due to their geographical location contributed to patients being adherent or non-adherent, whilst at the same time there were other factors affecting adherence irrespective of where the patients' geographical location was. Factors that promoted adherence the most in the deep rural area were safe and clean facility, good staff attitudes and the use of reminder aids. Factors that contributed towards poor adherence in the semi urban area included waiting time, not being granted leave from work, mistrust of the new single tablet, having no other caregiver at home, non-disclosure of status and feeling depressed.

Though many studies have been done on adherence and many interventions implemented, adherence to treatment is still not optimal. Therefore it is essential to monitor for adherence and to consistently measure patients' understanding of the importance of adherence. Educational interventions should be periodically carried out every 6 months in order to reinforce the importance of being adherent and preventing resistance to

medication. Identifying factors that contribute negatively to adherence due to patients' geographical location is important to hasten the end of the epidemic of HIV/AIDS in South Africa.

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CHAPTER 3

3. Synthesis

3.1 Discussion

3.1.1 The socio-demographic profile of the respondents

Of the 1020 patients, 623 (61%) were females and 397 (39%) were males. There was no association between gender and the level of adherence ($p=0.817$). Some authors have reported that there was no correlation between gender and adherence which affirms the findings from this study.¹⁹

The respondents were mostly in the youth category of 18-35 years ($n=580$; 56.9%). Other respondents ($n=439$; 43.1%) were middle aged. This signified majority to be of young, sexually active and reproductive group. In this study, there was no association found between adherence levels and age ($p=0.996$). This finding agrees with a study done by Weidle et al.²⁰

The majority of respondents being females, and the prevalence of HIV in the 18-35 age group is consistent with the 2012 survey which found that HIV prevalence amongst South African women was nearly twice as high as men,²¹ and that rates of new infections among women aged 15-24 were more than four times greater than that of men of the same age.²²

Weidle et al.²⁰ found that there was no association between marital status and adherence. This agrees with findings of this study ($p=0.601$).

In this study there was also no association found between the number of dependants of the respondents and adherence levels ($p=0.997$).

The majority of patients (49%) in all the 3 different areas of the study had secondary level of education. There is no significant association between educational levels and adherence to treatment. This concurs with the Weidle et al.²⁰ study which also found no association.

In this study, none of the demographic variables/personal factors showed significant association to the adherence levels of the respondents. This is consistent with studies done where socio-demographic factors generally did not predict adherence behaviour although some studies did find that male sex, white ethnicity, older age, higher income, higher education and literacy correlate with better adherence.²³

These findings show that demographic factors such as age, gender, marital status, educational level, etc as one of the modifying factors that modify a person's perception about a disease might not be predictors of or influence adherence to ART.²⁴

3.1.2 Level of adherence to ARV treatment and level of understanding of the importance of adherence

With respect to their understanding, although 80.9% of the respondents indicated that they understood the importance of adherence, an overall 58.5% were actually adherent to treatment, with the majority (89.4%) coming from the deep rural area ($p=0.001$) compared to the rural (52.9%) and semi urban (33.2%) areas. This raises concerns as all patients included in this study had been on treatment for more than 2 years and provision of HIV/AIDS education and counselling to the patients is continuously done at every encounter with the healthcare providers at the healthcare facilities. The practice of being adherent by these patients appears to be neglected even though they are knowledgeable about the importance. A further survey determining what they actually understand about adherence and its importance should be carried out to devise appropriate interventions to help the patients obtain optimal adherence to ART.

People taking antiretroviral medication and their supporters need to understand new and complex ideas around the medication itself, side effects, nutrition and positive living. Treatment literacy aims to help individuals and communities understand why ARV treatment is needed, and what it can and cannot do. Effective treatment literacy, developed by or with people living with HIV/AIDS and those taking ART, can lead to improved health outcomes, better adherence to drug regimens and higher uptake of health counselling and testing.

3.1.3 Factors affecting adherence to ARV treatment

3.1.3.1 Factors adversely affecting adherence

In terms of the factors that affect adherence to ARV treatment, the time of travelling between home and the facilities was significantly associated with the area of residence ($p=0.000$). A larger percentage of patients in the deep-rural and rural areas reported taking 2-3 hours to get to the facility having to travel a distance of 15 to 20km at a cost. In a study done in Botswana²⁵ it was reported that the cost incurred through transport to visit ART clinics was a major obstacle that had a negative impact on optimal adherence to ART. This concurs with results found in this study where distance travelled to health facilities impacts on the transport costs thus adversely affecting adherence due to the burden of paying for transport to ART sites.

The weather was significantly associated with the level of adherence to treatment ($p=0.000$). A much higher proportion of the deep-rural area patients (73.8%) associated the weather with their ability to collect medication from the health facility. Rainy weather makes it difficult to travel to ART sites from the deep rural area as rivers that are crossed on foot are sometimes full. Great discomfort is also caused by sunny weather for patients who walk to these facilities.

In terms of relating waiting time and adherence, there was a significant association noted between waiting time and adherence ($p=0.000$). A total of 635 (62.3%) patients waited in the queue for 2 hours and longer, with a significantly higher number of patients from the semi-urban ($n=296$; 87.1%)

area reported having waiting times of greater than 3 hours. A previous study found that patients who stayed in queues for a long time (4 hours or more) before being helped by service providers find it difficult to fulfil all appointments as they think about past experiences encountered at the health facility.²⁶

The death of a family member showed to have a statistical significance on level of adherence ($p=0.000$) and meeting their appointments. A total of 437 patients mentioned that family deaths affect them and hinders them from collecting their medication, with the highest number affected from the deep rural ($n=185$; 54.4%) area. This is due to cultural beliefs where limited mobility is part of the signs of mourning, mostly affecting African females who are expected to gather in a room with the grieving mother of the deceased. This probably accounts for over half of the patients (51.7%) missing between 2-4 appointments, the majority coming from the deep rural area.

Another contributory factor to missed appointments could be the availability or access to a caregiver. It was reported by about 25% ($n=253$) of patients that they are the only caregivers at home having to take care of their dependants. This influences the patient's availability to come to health facilities to collect their medication as the patients need to look for caretakers for their children on the day of collecting medication from ART sites. A greater proportion of these patients ($n=124$; 36.5%) were in the semi urban area where extended family system is not a common occurrence.

At the time of data collection for this study, all patients chosen for the study were issued with one month's supply of medication. The pharmacy refill date given to the patient ensures that patients collect their next supply in time while the patients have not run out of medication. Overall, 774 (75.9%) of patients in this study indicated that having sufficient stock at home allowed them not to collect their next supply. Having stock at home by the time of the next refill appointment meant respondents were not taking their medication accordingly hence denoting non-adherence.

A patient's mental wellbeing can greatly affect adherence as feeling depressed may influence whether or not the patients end up taking their medication as required.²⁷ There was a significant association between patients who felt depressed and adherence ($p=0.004$) in this study.

Half of the patients ($n=517$; 50.7%) in this study confirmed using traditional medicines, across all 3 areas of residence. Although there was no statistical significance, the influence of traditional healers and religious leaders undermined the evidence-based medical community's efforts to initiate and retain patients on ART, with dire morbidity and mortality consequences. Even after ART literacy classes, traditional beliefs outweighed faith in the healthcare system. The promise of a short-term, "curative" traditional remedy was more attractive than lifelong ART. Furthermore, traditional healer services were perceived by patients to be more attentive and individualized than clinic care, creating competition that discouraged ART.²⁸

Alcohol as a factor influencing adherence is cited in many studies^{29, 30}. In this study there was a statistical significance between alcohol use and adherence to medication ($p=0.000$). The reported use of alcohol was higher in the deep-rural area ($n=318$; 93.5%) than in the other areas, which was consistent with findings of a previous study.³¹

Although 25.4% of respondents in this study reported substance abuse having similarly affected respondents in all 3 areas, there was no association to adherence ($p=0.764$).

Family members' poor understanding of HIV and its transmission routes leads to stigmatization at home.²⁸ Even though patients accept their HIV diagnosis they are still afraid to disclose to family members and sexual partners their HIV status for fear of being blamed for one's HIV infection or threat of expulsion from the home.³² In this study, there was a statistical significance between non-disclosure of status and adherence ($p=0.008$). A larger proportion (62.4%) of patients who did not disclose their status was in the semi-urban area, which contributed to lower adherence levels seen in this area.

In South Africa, AIDS sickness is coupled with eligibility for disability grants, and patients are entitled to a state-funded monthly income because of their illness-related incapacity to work. However, widespread unemployment has meant that disability grants are an important and at times the only source of income, even if patients are well enough to work. When disability grants are tied to AIDS-related indicators, such as CD4 counts or viral load, non-adherence may become an attractive option for patients who fear losing their grant if their CD4 count were to increase.³³ There was an association found between the fear of loss of social grant and adherence to treatment ($p=0.000$). Seventy percent ($n=713$) of patients feared losing their grants if their CD4 cell count improved, with the greatest fear in the deep rural area (88.5%).

In this study 396 respondents were employed, with 308 (77.8%) having reported not being granted leave or time off from work to collect their medication. This impacts the patient's ability to collect medication from health facility during the working hours of the health facility. It was reported that costs incurred through lost wages to visit ART clinics were major obstacles to adherence, concurring with findings of a study done in Botswana.²⁵

Across all three regions, of the 623 (67%) patients on FDC in this study, a total of 413 respondents (66.3%) showed mistrust of the single FDC tablet. There was a significant association between the mistrust of the new single (FDC) tablet and adherence level ($p=0.023$). Hence education on the benefits of the FDC needs to be revised in order to allay their fears and mistrust.

In this study, pill burden was classified as those patients taking 4 or more tablets at a time. Pill burden affected 66.1% of all patients, the highest being in the semi-urban area (68.2%), although having shown no association between pill burden and level of adherence ($p=0.514$).

Changing medication in ART would be indicated as a result of severe side effects, drug interactions as a result of co-morbidity or that medications are failing to control the HIV virus. Medication failure as a reason for change is least in this study as only 6% (n=62) of patients in this study are on a second line regimen. There were no reported switches of medication from one first line regimen to the other, for patients who are still using single agents and are not on FDC.

Although no significant association was found between side effects and adherence (0.995), side-effects were raised by 67.9% (n=693) of patients as one of the reasons for non-adherence to treatment, with 36% having chronic rash, 22.2% with weight issues (weight gain or weight loss), 9.2% with lipodystrophy and 1% with gynecomastia.

The time of taking medication (i.e. morning, noon, afternoon, evening, night, morning and nighty) has no statistical significance (p=0.964). Those patients who are on fixed dose combination (FDC) medication preferred to take their medication at noon (n=351; 34.4%) and those on single agents (n=275; 27%) took their medication in the morning and night. Only 18.8% of patients taking single agent medication missed one of the daily doses of medication. Of these patients, 25.9% are from the semi-urban area. There was statistical significance between missed doses and adherence (p=0.000).

Feeling better was identified as a barrier to medication adherence in some patients.³⁴ This concurs with this study where over half of the patients (51.3%) did not sometimes see the need to take their medication due to feeling better. This generally affected patients in all 3 different areas of residence.

3.1.3.2 Factors promoting adherence

The level of cleanliness of the environment as well as the perceived security of the respondents while within the facilities where they felt safe were reasons cited by patients that encouraged them to visit their clinics. There was a significant association (p=0.000) between adherence and safety of the facility. Most of patients (n=876; 85.9%) felt safe in the health facility across all 3 areas which positively affected adherence. This may somehow be associated with facility preference. Facility preference was higher in the rural and deep rural areas thus positively influencing adherence to treatment in these areas.

Studies previously done showed that the absence of a good patient and healthcare provider relationship and the poor attitude of the healthcare team at health facilities can be a significant barrier to adherence.³⁵ In this study, staff attitude showed a significant association with adherence (p=0.000). Almost 60% of patients received good staff attitudes from healthcare workers in the 3 different facilities, the highest being in the deep-rural area (n=242; 71.2%). This concurs with the findings of this study which showed the highest percentage of adherent patients being in the deep-rural area.

Food insecurity may affect the regularity of ART doses, as some patients have reported taking their medication only when they have food available.³³ This impacts on adherence because ARV

medication cannot be taken on an empty stomach. There was a significant association between food availability and area of residence ($p=0.000$). Patients in the semi-urban area reported having food frequently available at home ($n=296$; 87%), compared to those in the rural ($n=100$; 29.4%) and deep-rural ($n=196$; 57.6%), yet surprisingly had the least level of adherence to treatment (33.2%).

A study done by Abdulrahman et al,³⁶ found that having daily reminders was one of the most important aids to taking medication on schedule. Taking medication on time positively affects adherence. In this study, there was statistical significance found between use of reminder methods and adherence levels ($p=0.002$). This affected patients equally in all the 3 different areas of residence.

3.2 Limitations

The study used a structured questionnaire which limited the possibility of in-depth understanding of the phenomenon under study since there were fixed responses to the questions that could not allow probing questions. With a survey, the accuracy of responses to the questions by respondents may be affected by recall bias. Adherence to long term therapy and its determinants is not a single incident but a continuous process over a period of time thus respondents may not be able to recall accurately their medication taking history.

3.3 Conclusion and Recommendations

More than half of the patients were adherent to treatment with the largest percentage residing in the deep-rural area, followed by rural then semi-urban area. Most factors due to their geographical location contributed to patients being adherent or non-adherent, whilst at the same time there were other factors affecting adherence irrespective of where the patients' geographical location was. Factors that promoted adherence the most in the deep rural area were safe and clean facility, good staff attitudes and the use of reminder aids. Factors that contributed towards poor adherence in the semi urban area included waiting time, not being granted leave from work, mistrust of the new single tablet, having no other caregiver at home, non-disclosure of status and feeling depressed.

Though many studies have been done on adherence and many interventions implemented, adherence to treatment is still not optimal. Therefore it is essential to monitor for adherence and to consistently measure patients' understanding of the importance of adherence. Educational interventions should be periodically carried out every 6 months in order to reinforce the importance of being adherent and preventing resistance to medication. Identifying factors that contribute negatively to adherence due to patients' geographical location is important to hasten the end of the epidemic of HIV/AIDS in South Africa.

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APPENDICES

Appendix 1: Information Sheet and Consent form

UKZN BIOMEDICAL RESEARCH ETHICS COMMITTEE

APPLICATION FOR ETHICS APPROVAL For research with human participants (Biomedical)

INFORMED CONSENT FORM FOR PARTICIPANTS

Information Sheet and Consent to Participate in Research

Date: _____

Hello, my name is Phumelele Mthethwa from the University of Kwazulu-Natal, School of Health Sciences, Discipline of Pharmaceutical Sciences. I am a researcher working under the University of Kwazulu-Natal. I can be contacted on 039 688 3046 / 0833148515 or emailed at phumelele.mthethwa@kznhealth.gov.za / phumelelen@yahoo.com. I am working on a research study entitled **“Measure of adherence to antiretroviral treatment amongst HIV positive patients attending antiretroviral clinics in selected rural, deep rural and semi-urban areas of KwaZulu-Natal”**

You are being invited to consider participating in a study that involves research. Before agreeing to participate, it is important that you read and understand the purpose of the study, the study procedures, benefits, risks and your right to withdraw yourself from the study at any time. You should not agree to take part unless you are satisfied about all the procedures involved. If you decide to take part in this study, you will be asked to sign and date this **Informed Consent Form** to confirm that you understand the study. You will be given a copy to keep.

THE AIM AND PURPOSE OF THE STUDY

The aim of the study is to find out what causes people who are on antiretroviral treatment not to collect and take their medication as instructed by their doctor/ pharmacist/ nurse at the hospital/ clinic they attend every month. The information that will be collected during the study will be used by the Department of Health to help in finding new systems and methods in improving adherence to treatment.

LENGTH OF THE STUDY AND NUMBER OF PARTICIPANTS

The study is expected to enroll a total of 1020 participants, with 340 patients being from a semi-urban hospital, 340 from a rural clinic or community health centre or hospital and 340 from a very rural clinic within Ugu District.

The study is expected to take 15-20 minutes of your time.

STUDY PROCEDURES

This facility has been selected to participate in the study a random. If you agree to participate in the study, the researcher will look at your medical records and ask you questions about you and how you take your treatment. The researcher will also ask you questions to find out the reasons for not taking your treatment in times where it was not taken. Answering these questions should take 15-20minutes of your time.

The study is funded by the School of Health Sciences of the University of KwaZulu-Natal.

CONFIDENTIALITY

We will not record your name or any other identifier so all information collected during the interview will be kept confidential. Results of this study will not be presented in a way that individual participants can be identified, however, results will be presented such that if there are differences in factors affecting adherence due to the location of the facility, it can be identified with that facility.

Your medical records of collection of treatment for the past year that will be reviewed to ascertain adherence to treatment will be kept confidential at all times. The interview that will be conducted with you to find out your reasons (if any) for not collecting and taking your medication will be done in a private room with only the researcher and you to ensure confidentiality of what is discussed.

Although every precaution will be taken to ensure confidentiality, absolute confidentiality cannot be guaranteed.

BENEFITS

There are no direct benefits to you today. However, the information collected during this study will be used by the Government, particularly the Department of Health, to help improve in finding new systems and methods in improving adherence to treatment.

You will not receive any compensation for participating in this study.

RISKS / DISCOMFORTS

This study has few risks for you to participate but will require some of your time. If you choose to participate in this study, you may refuse any questions that you do not want to answer.

If you are uncomfortable you may withdraw from the study without any penalties.

However, if answering the questionnaire is going to cause any psychological discomfort, please notify the data collector immediately who will escort you to a health professional for further management.

ETHICS APPROVAL

This study has been ethically reviewed and approved by the UKZN Biomedical research Ethics Committee (approval number_____). A copy may be obtained from me should you wish to review it.

WHAT DO I DO IF I HAVE QUESTIONS OR PROBLEMS?

In the event of any problems or concerns/questions you may contact the researcher (Phumelele Mthethwa, KZN Department of Health, Manager: Pharmaceutical Services, Ugu Health District Office, P/Bag x 735, Port Shepstone 4240, Tel: 039 688 3046, Cell: 0833148515, email: phumelele.mthethwa@kznhealth.gov.za / phumelelen@yahoo.com) or the UKZN Biomedical Research Ethics Committee, contact details as follows:

BIOMEDICAL RESEARCH ETHICS ADMINISTRATION

Research Office, Westville Campus
Govan Mbeki Building
Private Bag X 54001
Durban
4000
KwaZulu-Natal, SOUTH AFRICA
Tel: 27 31 2604769 - Fax: 27 31 2604609
Email: BREC@ukzn.ac.za

YOUR RIGHTS AS A PARTICIPANT

Your participation in this research is voluntary. You may withdraw your participation in the study at any time, without stating any reason. In the event of refusal/withdrawal of participation you will not incur penalty or loss of treatment or other benefit to which you are normally entitled.

You may come to the researcher physically or contact the researcher telephonically or by email to withdraw from the study, stating your name and the health facility that you were interviewed from.

No cost will be incurred by you as a result of participating in this study.

NEW FINDINGS

All new findings or any additional information that becomes available during the study, which may affect your willingness to continue in the study, will be made known to you as soon as possible.

CONSENT

I, _____, have been informed about the study entitled **“Measure of adherence to antiretroviral treatment amongst HIV positive patients attending antiretroviral clinics in selected rural, deep rural and semi-urban areas of KwaZulu-Natal”** by Phumelele Mthethwa, the researcher.

I understand the purpose and procedures of the study.

I have been given an opportunity to ask questions about the study and have had answers to my satisfaction.

I declare that my participation in this study is entirely voluntary and that I may withdraw at any time without affecting any treatment or care that I would usually be entitled to.

If I have any further questions/concerns or queries related to the study I understand that I may contact the researcher (Phumelele Mthethwa, KZN Department of Health, Manager: Pharmaceutical Services, Ugu Health District Office, P/Bag x 735, Port Shepstone 4240, Tel: 039 688 3046, Cell: 0833148515, email: phumelele.mthethwa@kznhealth.gov.za / phumelelen@yahoo.com).

If I have any questions or concerns about my rights as a study participant, or if I am concerned about an aspect of the study or the researchers then I may contact:

BIOMEDICAL RESEARCH ETHICS ADMINISTRATION

Research Office, Westville Campus
Govan Mbeki Building
Private Bag X 54001
Durban
4000
KwaZulu-Natal, SOUTH AFRICA
Tel: 27 31 2604769 - Fax: 27 31 2604609
Email: BREC@ukzn.ac.za

Signature of Participant

Date

**Signature of Witness
(Where applicable)**

Date

**Signature of Translator
(Where applicable)**

Date

Appendix 2: Questionnaire

PARTICIPANT'S DETAILS

PATIENT CODE:													
NAME OF FACILITY:		AGE:	GENDER:										
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M	F												
MARITAL STATUS:													
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M	S												
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A	I	W	C	other									
EDUCATIONAL STATUS/LEVEL:			MODE OF TRANSPORT:										
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Never attended	1°	2°	3°										
Private	Public	Lift Club	Foot	Other:									
DATE OF LAST CLINIC VISIT:			TODAY'S DATE:										
NO. OF MISSED VISITS/APPOINTMENTS:			DURATION OF PERIOD ON TREATMENT:										
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1-2YRS	2-3YRS	3-4YRS	4-5YRS	≥5 YRS									
ADHERENCE:													
<table border="1"> <tr> <td>Adherent</td> <td>Non-adherent</td> </tr> </table>					Adherent	Non-adherent							
Adherent	Non-adherent												

FACTORS AFFECTING ADHERENCE:

1.	I attended treatment literacy classes before starting treatment & I therefore, understand the importance of taking my treatment everyday					
				<table border="1"> <tr> <td>Yes</td> <td>No</td> </tr> </table>	Yes	No
Yes	No					
2.	Traditional medicine use					
	Never	Monthly	Weekly	Daily		
3.	Alcohol use					
	Never	Monthly	Weekly	Daily		
4.	I wait for public transport to / from the clinic/CHC/hospital for up to					
	0-1hr	1-2hrs	2-3hrs	>3hrs		
5.	The clinic/CHC/hospital is _____ from my house					
	<5km	5-10km	10-15km	15-20km >20km		
6.	Poor weather conditions					
				<table border="1"> <tr> <td>Yes</td> <td>No</td> </tr> </table>	Yes	No
Yes	No					

7.	Safety of place of collection					Good		Bad									
8.	I like the facility					Yes		No									
9.	Staff attitude & service at the facility					Good		Bad									
10.	Waiting time at the facility					0-1hr		1-2hrs		2-3hrs		>3hrs					
11.	Death in family / neighbourhood					Yes		No									
12.	No other caregiver at home					Yes		No									
13.	I had sufficient stock at home					Yes		No									
14.	Unable to attain leave from work during hours of operation of facility					Yes		No									
15.	I was feeling better so saw no need to collect medication					Yes		No									
16.	Taking the medication always makes me feel depressed					Yes		No									
17.	Reminder method (alarm/ Rx buddy/ Family/ Spouse/ Child) not effective					Yes		No									
18.	At what time of the day do you take your medication					morning		noon		afternoon		evening		night		morning & evening	
19.	Availability of food					Always available		Frequently available		Rarely available							
20.	I have too many pills to take					1-2pills		3-4pills		5-6pills		7-8pills		9-10pills		>10pills	

21.	I smoke /use drugs e.g wonger					Yes	No
22.	When I came to the facility last time/month there was no stock and could not come back					Yes	No
23.	My regimen changed and the new regimen makes me feel sick all the time					Yes	No
24.	Taking the medication has caused general physiological side effects						
	Chronic rash	Weight gain/loss	lipodystrophy	gynaecomastia	other		
25.	Fear of losing social grant when CD4 count measurement rises					Yes	No
26.	I have not disclosed my status to family due to stigma of HIV in the family & fear of discrimination					Yes	No
27.	I sometimes only remember to take my first dose of medication in the morning and forget to take my second dose of medication in the evening (OR vise versa)					Yes	No
28.	I have been taking my medication twice a day all along and I don't trust the new pill (one pill) taken once a day (FDC). So I stopped taking medication because I don't trust that it works as well as the old medication.					Yes	No

Appendix 3: BREC Approval Letter



20 February 2015

Mrs Phumelele Mthethwa
P.O. Box 30360
Richards Bay, 3900
phumelele@yahoo.com

Dear Mrs Mthethwa

PROTOCOL: Antiretroviral treatment among HIV positive patients attending antiretroviral clinics in selected rural, deep rural and semi-urban areas of Ugu District in KwaZulu-Natal: Degree Purposes (MMedSc). BREC REF: BE399/14.

EXPEDITED APPLICATION

A sub-committee of the Biomedical Research Ethics Committee has considered and noted your application received on 21 August 2014.

The study was provisionally approved pending appropriate responses to queries raised. Your responses received on 18 February 2015 to queries raised on 22 January 2015 have been noted by a sub-committee of the Biomedical Research Ethics Committee. The conditions have now been met and the study is given full ethics approval.

This approval is valid for one year from 20 February 2015. To ensure uninterrupted approval of this study beyond the approval expiry date, an application for recertification must be submitted to BREC on the appropriate BREC form 2-3 months before the expiry date.

Any amendments to this study, unless urgently required to ensure safety of participants, must be approved by BREC prior to implementation.

Your acceptance of this approval denotes your compliance with South African National Research Ethics Guidelines (2004), South African National Good Clinical Practice Guidelines (2006) (if applicable) and with UKZN BREC ethics requirements as contained in the UKZN BREC Terms of Reference and Standard Operating Procedures, all available at <http://research.ukzn.ac.za/Biomedical-Research-Ethics.aspx>.

BREC is registered with the South African National Health Research Ethics Council (REC-290408-009). BREC has US Office for Human Research Protections (OHRP) Federal-wide Assurance (FWA 678).

The sub-committee's decision will be **RATIFIED** by a full Committee at its meeting taking place on 10 March 2015.

We wish you well with this study. We would appreciate receiving copies of all publications arising out of this study.

Yours sincerely

Professor V Rambiritch
Deputy Chair: Biomedical Research Ethics Committee

Biomedical Research Ethics Committee

Professor D R Wassenaar (Chair)

Westville Campus, Govan Mbeki Building

Postal Address: Private Bag 254001, Durban 4000

Telephone: +27 (0) 31 260 2408 Facsimile: +27 (0) 31 260 4939 Email: brec@ukzn.ac.za

Website: <http://research.ukzn.ac.za/Biomedical-Research-Ethics.aspx>



Founding Colleges: Durban College Howard College Medical School Pietermaritzburg Westville

Appendix 4: Department of Health Approval Letter



health

Department:
Health
PROVINCE OF KWAZULU-NATAL

Health Research & Knowledge Management sub-component
10 – 103 Natalia Building, 330 Langalibalele Street
Private Bag x9051
Pietermaritzburg
3200
Tel.: 033 – 3953189
Fax.: 033 – 394 3782
Email.: hkrkm@kznhealth.gov.za
www.kznhealth.gov.za

Reference : HRKM23/15
NHRD Ref: KZ_2015RP14_225
Enquiries : Ms G Khumalo
Telephone : 033 – 395 3189

Dear Mrs P.P. Mthethwa

Subject: Approval of a Research Proposal

1. The research proposal titled 'MEASURE OF ADHERENCE TO ANTIRETROVIRAL TREATMENT AMONGST HIV POSITIVE PATIENTS ATTENDING ANTIRETROVIRAL CLINICS IN SELECTED RURAL, DEEP-RURAL AND SEMI-URBAN AREAS OF UGU DISTRICT IN KWAZULU-NATAL' was reviewed by the KwaZulu-Natal Department of Health (KZN-DoH).

The proposal is hereby **approved** for research to be undertaken at Ugu District.

2. You are requested to take note of the following:
 - a. Make the necessary arrangement with the identified facility before commencing with your research project.
 - b. Provide an interim progress report and final report (electronic and hard copies) when your research is complete.
3. Your final report must be posted to **HEALTH RESEARCH AND KNOWLEDGE MANAGEMENT, 10-102, PRIVATE BAG X9051, PIETERMARITZBURG, 3200** and e-mail an electronic copy to hkrkm@kznhealth.gov.za

For any additional information please contact Ms G Khumalo on 033-395 3189.

Yours Sincerely

Dr E Lutge
Chairperson, Health Research Committee

Date: 18/02/15

uMnyango Wezempilo. Departement van Gesondheid
Fighting Disease, Fighting Poverty, Giving Hope

Appendix 5: Permission to conduct study at Ugu District facilities



Department:

Health

PROVINCE OF KWAZULU-NATAL

UGU HEALTH DISTRICT OFFICE

41 Bisset Street, via Entrance of Nelson Mandela Drive, Port Shepstone 4240

P/Bag x 735, Port Shepstone 4240

Tel: 039 688 3000

Fax: 039 682 6296

E-mail: veeran.chetty@kznhealth.gov.za

www.kznhealth.gov.za

Enquiries: Mr V Chetty
Ref: UGUDHO Research
Date: 12 August 2014

Principal Investigator: Mrs. P.P. Mthethwa
Manager: Pharmaceutical Services
Ugu Health District Office

Re: PERMISSION TO CONDUCT RESEARCH AT UGU DISTRICT HEALTH FACILITIES

I have pleasure in informing you that permission has been granted to you by the District Office/Facilities to conduct research on "Measure of adherence to antiretroviral treatment amongst HIV positive patients attending antiretroviral clinics in selected rural, deep-rural and semi-urban areas of Ugu District in Kwazulu-Natal."

Please note the following:

1. Please ensure that you adhere to all the policies, procedures, protocols and guidelines of the Department of Health with regards to this research.
2. This research will only commence once this office has received confirmation from the Provincial Health Research Committee in the KZN Department of Health.
3. Please ensure that this office is informed before you commence with your research.
4. The District Office/Facilities will not provide any resources for this research.
5. You will be expected to provide feedback on your findings to the District Office/Facilities.

Thanking you.

Sincerely

Mr Veeran Chetty
District Manager
Ugu Health District Office

Zertifikat Certificat

Certificado Certificate

Certificat de formation - Training Certificate

Ce document atteste que - this document certifies that

Phumelele P. Mthethwa

a complété avec succès - has successfully completed

Module 1

du programme de formation TRREE en évaluation éthique de la recherche
of the TRREE training programme in research ethics evaluation

December 11, 2013

CD : 000007106

Professeur Dominique Sprumont
Coordinateur TRREE Coordinator

FMH

Continuing Education Program (3 Credits)
Programme de Formation Continue (3 Crédits)

Federale
Pharmaceutica
Instituut

FPH

Programme de formation
continue

Continuing Education Program
Programme de Formation Continue

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Swiss Academy of Medical Sciences (SAMS) (www.sams.ch) - Commission for Research Partnership with Developing Countries (www.crdp.ch)

(321) - 00110817