Linkage to HIV care from a mobile testing unit in South Africa by different CD4 count strata

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Cape Town, 2011

DECLARATION

MPH (Epi) Mini-Dissertation

I _____Student No._____

declare that the work that I have submitted is my own and where the work of others has been used (whether quoted verbatim, paraphrased or referred to) it has been attributed and acknowledged.

Signature: _____ Date: _____

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ABSTRACT

Delayed presentation for antiretroviral therapy (ART) care is common in sub-Saharan Africa, with most patients accessing care when immunocompromised and a high proportion dying in their first year of ART. These shortcomings are hindering the success of ART programmes, and solutions to mitigate this problem, lie further upstream between the interval of HIV testing and ART initiation.

The aim of the literature review (Part B) was to assess retention and linkage at each stage between HIV testing and ART initiation and to identify risk factors, barriers and facilitators influencing each stage between this interval.

Timely entry into HIV/ART care is crucial to achieve maximum health benefits for the patient and healthcare system. The aim of the research study (Part C) was to assess the proportion and characteristics of newly-diagnosed HIV+ patients who received their laboratory CD4 count result and accessed HIV care after testing HIV+ at a mobile testing unit as well as to examine barriers to HIV care. The study was based on the hypothesis that linkage to care among HIV+ individuals with lower CD4 counts would be better in comparison to those with higher CD4 counts. The protocol (Part A) outlines the study design and procedures.

Findings from the literature review (Part B) indicated that substantial attrition occurred at all steps between the interval of HIV testing and ART initiation. The first major drop-out occurred at the point of linkage from a HIV testing site to a medical facility for ongoing care. The next loss occurred between CD4 count testing and collection of the test result. Moreover, this review found that less than half of the patients not yet eligible for ART were retained in pre-ART care (range: 42%-45 %) and nearly two-thirds of ART-eligible patients linked to ART care (median: 67%, IQR 58-81).

Results from the study (Part C) showed that forty-three (27%) individuals did not receive their CD4 count result. A lower CD4 count, being female and the availability of a phone number increased the likelihood of receiving this result. Linkage to care was 100% in patients with CD4 counts ≤ 200 cells/µl, 66.7% in individuals with CD4 counts of 201-350 cells/µl and 36.4% in those with CD4 counts > 350 cells/µl. A lower CD4 count, disclosure, presence of TB symptoms and unemployment increased the likelihood of linking to care. The most common stated barrier (41.4%) to linking to care was the inability to access public healthcare facilities during working hours.

Interventions such as structured referral systems, transport vouchers, community escorts, point of care (POC) CD4 count testing and effective post-test counselling could reduce drop-out between HIV-testing and ART initiation. Linkage to care was best among those eligible for ART. Interventions designed at improving linkage among employed individuals are urgently warranted.

PART A: PROTOCOL

Note to examiner: Only data forms pertaining to the study have been presented in the Appendix. Data forms used by the mobile unit have not been included as they are part of an ongoing service.

PART A: PROTOCOL

SYNOPSIS

AIM

The aim of this study is to investigate the linkage of newly-diagnosed HIV positive clients from a mobile testing unit (Tutu Tester) to HIV care at public healthcare facilities as well as to investigate the reasons for not linking to care.

OBJECTIVES

The primary objectives are to 1) determine the proportion of newly-diagnosed HIV positive clients who were assessed for antiretroviral therapy (ART) eligibility and received their laboratory CD4 count result from the mobile unit, 2) measure the proportion of newly-diagnosed HIV positive clients that accessed a primary healthcare facility, 3) document the proportion of newly-diagnosed HIV positive clients eligible for ART that subsequently started ART and 4) to establish the median time from diagnosis to entry into care for ART-eligible clients and clients not yet eligible for ART. Furthermore, the secondary objective is to investigate the reasons for not linking to care.

STUDY DESIGN

This is a prospective observational cohort study which will involve following up (telephonically or home visits) clients that were newly-diagnosed with HIV within the Cape Metropolitan district, between August 2008 and December 2009, and successfully contacted to receive their laboratory CD4 count result. Client records of all potentially eligible participants will be reviewed by staff subsequent to obtaining informed consent. Participants will undergo a brief questionnaire session and thereafter a clinic folder review will be conducted on patients that linked to care and provided additional consent to access their folders in order to verify self-reports.

PART I) INTRODUCTION

1.1) Background

The generalised HIV/AIDS epidemic in South Africa has undoubtedly reached catastrophic levels. HIV prevalence in adults aged 15-49 was estimated to be 18.1% in 2008 in South Africa. [1] Remarkable progress has been made with regards to antiretroviral therapy (ART) roll-out in resource-limited settings. [2] However, in 2007 an estimated 350 000 deaths were attributable to HIV/AIDS in South Africa. [1] Delay of ART initiation is thought to result in high HIV associated mortality and morbidity. [3] Hence efforts to ensure that HIV-infected individuals initiate care and treatment promptly are vital to achieve better outcomes.

1.2) HIV testing and counselling: A gateway to prevention, care, treatment and support

HIV testing and counselling should be the entry point to a continuum of HIV care. The South African National Strategic Plan aims to provide access to appropriate packages of care, treatment and support to 80% of all the people diagnosed with HIV by 2011 in order to reduce mortality and morbidity. [4] According to South Africa's HIV/AIDS Operational Plan, once an individual is diagnosed with HIV, assessment for ART eligibility including a CD4 count and clinical staging should follow promptly. [5] HIV-infected individuals who are not yet eligible for ART should be advised to enter comprehensive HIV care whereas those with a laboratory CD4 count <200 cells/µl or clinical stage 4 should be referred for starting ART. [5] Once HIV-infected individuals have had their first contact with the primary healthcare facility they should enter a continuum of care which might include ART and/or Cotrimoxazole, regular screening for cervical cancer, intensified tuberculosis (TB) case finding and contraceptives.

Limited data investigating the proportion of newly-diagnosed HIV infected individuals assessed for ART eligibility [6] and the proportion of ART-eligible individuals promptly starting ART is available.[7] A recent study looking at routinely collected data from HIV testing and treatment facilities in Mozambique showed that of the 1506 adults eligible for ART, only 471 (31.3%) started ART. [8] A study conducted in South Africa found that of the 501 patients eligible for ART in an urban hospital setting; only 408 patients (81.4%) were in care and on ART at 3-month follow-up in Durban .[7] A study conducted in Cape Town in 2006 concluded that only 60% of newly-diagnosed HIV positive clients had a CD4 count within 6 months of diagnosis. [6] In contrast, loss to follow-up in ART cohorts is well described. To date, several studies from sub-Saharan Africa have documented a substantial early loss to follow-up and mortality of patients in ART programmes [9] but only a few studies have reported on these indicators before patients initiate treatment and care. [7]

1.3) Justification and Hypothesis

There is a paucity of published studies from resource-limited settings investigating the linkage of newly-diagnosed HIV positive individuals to comprehensive HIV care. Furthermore, the linkage of HIV testing and care in mobile testing settings is an area of research that remains to be explored. The impetus for undertaking this research is to fill this gap and provide insight in the link to HIV care and treatment at primary healthcare facilities after accessing a mobile testing service.

The Tutu Tester has been in operation for more than 18 months. The service is ongoing. It is our belief that this service could be enhanced if we knew the extent of linkage to care by clients who test positive for HIV. It is our hypothesis that this may be relatively good in patients with low CD4 counts or concomitant disease but less good in patients who are earlier in their infection. The client's stage of infection at diagnosis is graphically presented to him/her during post-test counselling using a colour coding system on a Road to HIV Health card that is offered to all clients. It would be important to know this baseline data in order to devise more intensive methods to improve linkage to care. This is particularly important with the prospect of earlier ART.

1.4) Study Site: The Tutu Tester

The Tutu Tester project is a mobile testing service managed by the Desmond Tutu HIV Foundation (DTHF). Apart from HIV testing and counselling, the Tutu Tester also offers diagnostic services for other conditions (i.e. hypertension, diabetes, obesity, TB, pregnancy) in an effort to normalise HIV testing. The Tutu Tester operates in and around the Cape Peninsula, in co-operation with the City of Cape Town and Provincial Health Authorities, usually at taxi ranks, shopping centres, other community facilities and along roadside. All services offered by the Tutu Tester are free of charge.

Each client accessing the mobile is first registered manually, providing only their date of birth, gender and initials. Thereafter the client's information is registered electronically and additional details such as residential suburb, nationality and cell phone number are stored. The client's fingerprint is also captured using the biometric system to facilitate access to their medical records at a subsequent visit. This electronic system generates a client code which is assigned to the individual. This code consists of four letters (indicating the site that the client was tested at) and a four digit number (sequential at each site). All personal details supplied by the client are voluntary and refusal does not influence client care in any manner. However, should the need arise only clients that give the Tutu Tester staff permission to be contacted are traced. Following registration the client's weight and height is measured. The client then sees a clinical nurse practitioner who

performs the HIV test, documents the medical history and measures the client's blood pressure and blood glucose.

The HIV testing model used by the Tutu Tester is client-initiated counselling and testing, in accordance with the provincial Advise, Consent, Test and Support (ACTS) policy. All clinical nurse practitioners and counsellors of the Tutu Tester have been trained in ACTS. Clients who consent to HIV testing undergo a rapid HIV test (Bioline HIV-1/2 3.0, Standard Diagnostics, Korea). A rapid confirmatory test (Determine HIV-1/2, Abbott Laboratories) is only performed if the first rapid test produces a positive result. Clients who test negative are subsequently tested for all other conditions and then undergo risk reduction counselling. Moreover referral letters are given to clients to take to their nearest healthcare provider if necessary. Clients who test positive are staged according to the World Health Organisation (WHO) staging manual. In addition, CD4 count testing is offered. This entails drawing a sample of blood which is then sent to Toga Laboratory in Gugulethu. Once an HIV test is done, the client undergoes testing for all the other conditions offered.

Furthermore, all HIV positive individuals, those with symptoms of TB and randomly selected individuals are asked to consent to doing an induced sputum sample as part of a study investigating active case finding (Rec Ref 502/2008). Induced sputum samples for TB testing are sent to the National Health Laboratories (NHLS) at Groote Schuur Hospital.

Thereafter HIV positive clients are given a referral letter to take to their healthcare provider together with a Road to HIV Health Card. The Road to HIV Health Card was designed by the DTHF and the Tutu Tester project in order to assist positive clients and nurses at their clinics with the virologic and immunologic monitoring of this disease by plotting viral loads together with the client's CD4 counts. Thus the primary aim of this intervention is to assist HIV positive clients in taking the responsibility of personally keeping track of their health condition.

When laboratory CD4 counts become available (usually within 72 hours) clients are contacted telephonically with their results and later with TB results. If contact numbers are unavailable either a home visit is done or a letter is sent to the address provided by the client, requesting the client to contact the Tutu Tester for their results. Once contact is made, the laboratory CD4 result is given and implications discussed. All HIV positive clients are requested to document their laboratory CD4 count result on their Road to HIV Health Card and encouraged to attend clinics for either comprehensive HIV care or to start ART if eligible, as well as other health services if necessary. In addition, clinics are also requested to contact the Tutu Tester for laboratory results. This follow-up process is well documented on the client's Tutu Tester follow-up form.

1.5) Study Aims and Objectives

1.5.1) Aims

The aim of this study is to investigate the linkage of newly-diagnosed HIV positive clients from a mobile testing unit to HIV care at public healthcare facilities as well as to investigate the reasons for not linking to care.

1.5.2) Objectives

- **Primary Objectives**
  1) To determine the proportion of newly-diagnosed HIV positive clients that received their CD count result from the mobile service.
  2) To determine the proportion of newly-diagnosed HIV positive clients that received their CD count result and accessed a health care facility for respective care.

- **Secondary Objectives**
  1) To investigate the reasons for not linking to care.

PART II) METHODS

2.1) Study Design

This is a prospective observational cohort study which will focus on Tutu Tester clients who were newly-diagnosed with HIV within the Cape Metropolitan district between August 2008 and December 2009 and successfully contacted to receive their laboratory CD4 count result. The period of follow-up is three months, April to June 2010. This process will involve obtaining informed consent, followed by the administration of a semi-quantitative questionnaire, either telephonically or face-to face, as well as contacting clinics to verify attendance.

2.2) Population and Sampling

2.2.1) Description of the population

The study will follow a cohort of Tutu Tester clients that were newly-diagnosed with HIV within the Cape Metropolitan area between August 2008 and December 2009 and successfully contacted to receive their laboratory CD4 count result. A major limitation in this study is the exclusion of newly-diagnosed HIV positive clients that were unable to be contacted from this cohort. This decision was taken as these clients did not receive feedback from the Tutu Tester on their assessment for ART eligibility based on a laboratory CD4 count result either due to laboratory error or because the Tutu Tester staff were unable to contact them.

- **Inclusion Criteria**
  - Newly positive HIV test performed at the Tutu tester between August 2008 and December 2009 within the Cape Metropolitan area
  - Available laboratory CD4 count result
  - Successfully contacted to receive laboratory CD4 count result
  - Aged 18 years or older
  - Able and willing to provide informed consent

- **Exclusion Criteria**
  - Known HIV positive clients
  - Aged less than 18 years old
  - Unable to provide informed consent

2.2.2) Sampling strategy, sample size and justification for sample size

The sample size for potentially eligible participants is 225. This estimate was ascertained from the Tutu Tester Access database and represents all Tutu Tester clients that were newly-diagnosed with HIV within the Cape Metropolitan area between August 2008 and December 2009 and successfully contacted to receive their laboratory CD4 count result. Stratification of this sample size according to laboratory CD4 count results reveals the following, 29 clients with CD4 counts less than 200 cells/µl, 48 clients with CD4 counts between 200-350 cells/µl and 148 clients with CD4 counts greater than 350 cells/µl. All clients with CD4 counts below 350 cells/µl will be included in this study. A random sample of 80 clients will be selected from the 148 clients with CD4 counts above 350 cells/µl due to budget constraints, a short study time period and feasibility. Hence the estimated sample size for this study is 157.

The majority of newly-diagnosed HIV+ individuals diagnosed on this mobile unit have CD4 counts > 351 cells/µl. [10] It is logistically unfeasible to follow-up all potentially eligible patients in the > 351 cells/µl CD4 count stratum within 3 months and thus a random sample (30%) will be drawn from this stratum. The proposed relatively small sample size in the < 200 cells/µl stratum and 201-350 cells/µl stratum is logistically manageable to follow-up within 3 months and thus it was decided that a 100% of individuals with laboratory CD4 counts ≤ 350 and 30% of individuals with laboratory CD4 counts > 350 cells/µl will be sampled.

2.3) Procedure

The Tutu Tester database, client forms, referral letters and follow-up forms will be used to retrieve specific information of all potentially eligible participants for the Client Form Reviews (Appendix 2). Thereafter these participants will be contacted to determine if they are willing to participate in this study and provide informed consent (Appendix 1). Up to 3 attempts will be made to contact the client. Where no telephone number is available, a home visit will be done. All participants providing informed consent will subsequently undergo a semi quantitative questionnaire session (Appendix 3). Note follow-up (telephonic and home visits) will be conducted in accordance with the Tutu Tester's Standard Operating Procedures (SOPs) for follow-up. Clinics will then be contacted to verify information supplied only by those participants who consent to this additional process (Appendix 1) and these details will be documented in the Clinic Attendance Form (Appendix 4).

2.4) Data collection and monitoring

Client data for each participant will be retrieved from the Tutu Tester Access database and subsequently checked for accuracy by reviewing client forms. All information entered into the Client

Form Review (Appendix 2), Questionnaire (Appendix 3) and Clinic Attendance Form (Appendix 4) will be quality controlled and subsequently double-entered onto an electronic database, EpiData. This database will be checked regularly for inconsistencies.

2.5) Staff

This research is being conducted by the staff running the Tutu Tester. The staff member primarily concerned is a PEPFAR fellow who is also reading for a Masters in Public Health and will investigate this subject for her thesis. Her work commitment on the Tutu Tester team involves quality control of data forms as well as obtaining laboratory CD4 count results and ensuring results are returned to positive clients.

An HIV/AIDS counsellor from the Tutu Tester Project will undertake the role of field worker for this study as this individual possesses adequate experience in adherence counselling, following-up (home visits and telephonically) of HIV positive clients and is well trained in Good Clinical Practice (GCP). The field worker will possess a good understanding of the protocol, study methodology and the importance of consent. The Masters student will conduct interviews with all clients wishing to communicate in English whereas the fieldworker will conduct interviews with Xhosa speaking participants.

2.6) Measurements: Outcome variables

Variable	Type	Definition	Data Source
• **Contactable**	Categorical: Binary Yes or No	A client that successfully received his/her laboratory CD4 count result from the Tutu Tester via the following methods: telephonically, face-to-face, via a clinic	▪ Tutu Tester database, client and follow-up form ▪ Client Form Review
• **Accessed care**	Categorical: Binary Yes or No	A participant that initiated care by attending a primary healthcare facility at least once after being tested on the Tutu Tester.	▪ Questionnaire ▪ Clinic Attendance Form
• **In care**	Categorical: Binary Yes or No	A participant that had visited a primary healthcare facility more than once in the last six months and is either in routine HIV care or commenced ART.	▪ Client Form Review ▪ Questionnaire ▪ Clinic Attendance Form
• **Eligible for ART and started ART**	Categorical: Binary Yes or No	A participant that had a laboratory CD4 count result of <200 cells/µl or clinical stage of 4 and is taking antiretrovirals (ARVs)	▪ Client Form Review ▪ Questionnaire ▪ Clinic Attendance Form
• **Not eligible for ART and in comprehensive HIV care**	Categorical: Binary Yes or No	A participant that did not have a laboratory CD4 count result of <200 cells/µl or clinical stage of 4 and is currently in routine HIV care and treatment (i.e. any of the following: had a CD4 count in the past 6 months, on Bactrim (Co-trimoxazole) and/ or INH prophylaxis, screened for TB/STIs, if female, had a pap smear in the last 6 months)	▪ Client Form Review ▪ Questionnaire ▪ Clinic Attendance Form
• **Not linked to care**	Categorical: Binary Yes or No	A participant that did not visit a primary healthcare facility after the Tutu Tester follow-up for purposes of HIV care.	▪ Client Form Review ▪ Questionnaire ▪ Clinic Attendance Form

2.7) Facilitation of clinic site preparation and participation

Several major clinics within the Cape Metropolitan region (i.e. Hout Bay Main Road Clinic, Masiphumelele Clinic, Vuyani Clinic, Nyanga Clinic, Lotus River Clinic, and KTC Clinic) are likely to be involved in this study as they are the Tutu Tester's main referral sites. Support from clinics is essential in order to access patient records for completion of this study's Clinic Attendance Form. Prior to contacting clinics, clinic managers will be issued with the study's protocol and requested to contact us if they have any queries relating to the clinic's involvement. More importantly, to minimise any disruption on facility functioning the clinic manager will be requested to schedule appointments for the study staff to contact the clinic clerk in order to retrieve the necessary information from patient folders. No information other than what is needed to complete the Clinic Attendance form will be obtained from the patient's folder.

PART III) ANALYSIS

3.1) Statistical Analysis

Data will be statistically analysed using Stata (Version 10.0, College Station, Texas, USA). All participants will be stratified according to laboratory CD4 count results (<200 cells/µl, 200-350 cells/µl, >350 cells/µl). Data will first be explored using simple tabulation and chi square statistics. The following proportions will be tabulated for each stratum:

1) The proportion of newly-diagnosed HIV positive Tutu Tester clients who were assessed for ART eligibility and received their laboratory CD4 count result from the mobile unit.
2) The proportion of newly-diagnosed HIV positive Tutu Tester clients that accessed a primary healthcare facility.
3) The proportion of newly-diagnosed HIV positive Tutu Tester clients eligible for ART that subsequently started ART.
4) The median time from diagnosis to entry into care for ART-eligible clients and clients not yet eligible for ART.

The following variables (i.e. age, sex, referral for other services, TB symptoms) will be tabulated against the outcome variables (receipt of laboratory CD4 count result and linkage to care) and compared across the three strata. Participants eligible for ART will be compared to those not yet eligible for ART. The association between linkage to care and possible determinants (i.e. age, sex, clinical staging, employment status, participant's perception of health status) will be determined using chi-square tests. The time from diagnosis to entry into care among ART-eligible clients and clients not yet eligible for ART will be assessed using medians and interquartile ranges.

Initial analysis will use bivariate predictors of receipt of laboratory CD4 count result and linkage into care, with variables significant at the $p<0.05$ level entered into a multivariate logistic regression model to determine independent predictors of each outcome.

Part IV) ETHICS AND COMMUNICATION

HUMAN SUBJECTS PROTECTION

All the procedures described here will be reviewed by the University of Cape Town Research Ethics Committee.

4.1) Information Sheet and Informed Consent Forms

The translated versions of these forms will be checked to verify all information before conducting any study procedures. Potential eligible participants will be contacted either telephonically or face-to-face to obtain informed consent (Appendix 1) which will be provided in the language understood by the prospective participant (English or Xhosa). Refusal to give additional consent to the verification process will not affect the participant's rights. This study adheres to the declaration of Helsinki 2000.

4.2) Subjects Confidentiality

Every effort will be put in place to maintain participant's confidentiality. This study will manage potentially sensitive issues, such as confidentiality by conducting follow-ups in accordance with the Tutu Tester SOP. Individual identifiers such as names will be stripped off all forms (i.e. Client Form Reviews, Questionnaires, and Clinic Attendance Forms). These forms will be identified by the participants study numbers and stored in locked file cabinets with restricted access at the Tutu Tester office in Silvertown, Cape Town. Forms with personal identifiers such as the Informed Consent will be stored in a similar fashion yet in a separate cabinet. Furthermore, the database will be stored on a data server located at the DTHF, secured with a password to limit access. Confidentiality agreements will be signed by personnel authorised to access records.

4.3) Potential Risk

A foreseeable harm could be the loss of participant's confidentiality. All personnel involved in this study will ensure that measures which minimize this risk will be maintained at all times. Participants may feel uncomfortable to be either visited at home or contacted telephonically. However, all study procedures will be conducted in the participants preferred method of contact. This study will in no way alter the clinical management of participants.

4.4) Dissemination and Implementation of Research Findings

The work will be prepared by the Masters student's for her thesis submission to the University of Cape Town- Department of Public Health and Family Medicine. A summary of findings will be disseminated to the respective clinics involved in this study. Furthermore, a full final report will be submitted to the City of Cape Town Health Department as well as the Western Cape Provincial

Department of Health. In addition, a research paper will be submitted for publication to a peer-reviewed medical journal and abstracts will be submitted to conferences.

Our main intention is to use the results from this study to devise a new model aimed at assisting HIV infected individuals link to care more efficiently if indeed the study shows inadequate linkage to care in the present model. The data, specifically reasons participants give for not linking to care, will provide us with the insight needed for designing this model, which we plan to pilot in the next phase of the Tutu Tester project.

PART V: LOGISTICS

5.1) Timetable

PHASE AND PERIOD	ACTIVITIES
PHASE 1: PREPARATION ▪ **MARCH 2010**	➢ Translate the information sheet and informed consent to Xhosa and verify translated version. ➢ Print data forms ➢ Set up data base ➢ Prepare fieldworker for study ➢ Create a list of potentially eligible participants
PHASE 2: FIELD WORK ▪ **APRIL –JUNE 2010**	➢ Follow-up on clients ➢ Contact clinics
PHASE 3: DATA ENTRY AND ANALYSIS ▪ **JULY-SEPTEMBER 2010**	➢ Quality control forms ➢ Enter data onto EpiData ➢ Verify accuracy of data entered ➢ Statistically analyse data
PHASE 4: WRITE-UP ▪ **OCTOBER-DECEMBER 2010**	➢ Write-up ➢ Submit draft to supervisor and co-supervisor by December
PHASE 5: EDITING ▪ **JANUARY 2011**	➢ Edit necessary changes to paper
PHASE 6: DISSEMINATION OF RESULTS ▪ **FEBRUARY- APRIL 2011**	➢ Submission of thesis ➢ Submission of full research report to City of Cape Town Health Department as well as the Western Cape Provincial DOH ➢ Submission of summary of findings to clinics involved ➢ Submission of research paper to peer reviewed medical journals and abstract to conferences
PHASE 7: IMPLEMENTATION OF RESULTS ▪ **MAY –JUNE 2011**	➢ Devise new model if applicable ➢ Pilot new model

5.2) Budget

This study will be funded by the foundation's French AID budget.

	Currency (ZAR)
PERSONNEL:	
Fieldworker (4500 x 3 months)	**13 500**
Personnel - Subtotal	**13 500**
OTHER:	
Translation (1 x Information Sheet & Informed Consent Form)	**1000**
Printing (1 x Information Sheet & Informed Consent Form, 1 x Client Form Review, 3 x Questionnaire, 1 x Clinic Attendance form @ 40 cents per pg)	**500**
Fuel (750 x 3 months)	**2 250**
Telephone/ Cell phone costs (1500 x 3 months)	**4500**
Local office costs (300 x 4 months)	**1200**
Other - Subtotal	**9450**
SUBTOTAL	**22 950**
TOTAL COSTS	**22 950**

PART VI: REFERENCES

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PART B: LITERATURE REVIEW

THE HIV CASCADE IN SUB-SAHARAN AFRICA: FROM HIV TESTING TO PRE-ART AND ART CARE

Note to examiner: *This literature review was updated during the course of this year as new studies around this topic were recently published. Findings from my study (Part C) were presented at the 18th Conference on Retroviruses and Opportunistic Infections (CROI), February 2011. The published conference abstract was included in the literature review (Part B) and in theory should be presented after my article (Part C). However, my literature review (Part B) is presented before the article (Part C) in accordance with the MPH dissertation guide*

PART B: LITERATURE REVIEW

1) INTRODUCTION

Sub-Saharan Africa continues to have the highest HIV/AIDS prevalence in the world with an estimated 22.5 million HIV-infected adults and children.[1] This region's generalised epidemic warranted rapid scale-up of HIV testing and antiretroviral therapy (ART) and thus by 2004 roll-out of testing sites and ART programmes commenced.[2] Despite the gains in expanded services, ART coverage remains considerably low (37%).[2] Furthermore, delayed presentation for ART care is common, with patients accessing care when immunocompromised and between 8%-26% of patients dying in their first year of ART.[3] These shortcomings are hindering the success of ART programmes, and solutions to mitigate to this problem, lie further upstream between the interval of HIV testing and ART initiation.[3]

The HIV cascade (i.e. the process between HIV testing through to ART initiation) is a synchronised pathway with a series of intermediate steps (Fig 1A). It begins with an HIV+ diagnosis, followed by completion of CD4 count testing and clinical staging.[4] Patients that meet the ART eligibility criteria usually enrol into a treatment readiness programme before commencing ART.[4] Those patients that are above the ART eligibility threshold (ART-ineligible) should enrol in a wellness programme and must remain in pre-ART care until they meet the ART-eligibility criteria. [4] This HIV cascade requires a well co-ordinated health system to facilitate linkage to care. However, in resource-constrained settings, inadequate healthcare systems frequently impede on a patient's transition through the system and thus attrition along this pathway is inevitable. Losses can readily occur at the point of baseline CD4 count testing, pre-ART or ART care enrolment, pre-ART retention and ART initiation. For patients testing at non-healthcare facilities drop-out can occur further upstream (i.e. between an HIV+ test result and registration at an HIV clinic for follow-up care) (Fig 1B).

Results from a recent mathematical modelling study suggests that retention of ART-ineligible patients in pre-ART care will be beneficial for resource-poor setting as it could increase the average life-years saved.[5] Thus quantifying the magnitude of attrition at every stage of the cascade is crucial for determining where interventions should be targeted to improve retention. A deeper insight into the factors impeding a patient's flow through the system is valuable for informing the design of these interventions.

To this end, the aim of this review is to assess each stage of the HIV cascade. The objectives are to: **1)** describe the proportion of eligible HIV+ patients retained in the appropriate form of care at each stage (Fig 1A): a. enrolled in HIV care following an HIV+ diagnosis, b. underwent CD4 count testing following diagnosis, c. received a CD4 count result following CD4 testing, d. enrolled in pre-

ART care if ART-ineligible and e. initiated ART if ART-eligible, **2)** highlight risk factors associated with retention or attrition at each stage and **3)** synthesise barriers and facilitators along the cascade.

2) METHODS

2.1) Criteria for selection of studies

The aim of the search strategy was to identify all studies reporting on the proportion of HIV+ patients at any one of the steps between HIV testing and ART initiation (i.e. the proportion of individuals that registered at a medical facility following an HIV+ test result, underwent baseline CD4 count testing following enrolment, received CD4 count results following CD4 testing as well as the proportion of ART-ineligible patients who were retained in pre-ART care and the proportion of ART-eligible patients that initiated ART) (Fig 1A-B). All studies reporting on risk factors, barriers and facilitators of linkage to HIV care through to ART initiation were also gathered. Barriers were defined as any reason for drop-out from the cascade whereas facilitators were defined as any intervention shown to link or retain patients along the cascade.

Studies were omitted if they: examined steps downstream from ART initiation (such as retention or adherence), were based on the private healthcare sector and were editorials or case-reports. Studies that were found to be of poor methodological quality were excluded. No restriction was placed on sample size. The search was limited to studies conducted within sub-Saharan Africa which were published in English between 2000 (the time when ART first became available in this region) [2] till the search end period (May 2011).

2.2) Search strategy

Two electronic databases (MEDLINE and Global Health) were comprehensively searched using a compound search strategy (Fig 2).

Keyword searches were then performed in Africa-Wide Information and Google Scholar. Thereafter reference lists of eligible studies were searched to ensure relevant papers were not missed. A keyword search was then performed in the dissertation database of the University of Cape Town to identify unpublished work.

Conference abstracts were sought through online abstract databases of the Conference on HIV Pathogenesis and Treatment of the International AIDS Society (IAS, 2001-2009), the Conference on Retroviruses and Opportunistic Infections (CROI, 2006-2011), the International AIDS Conference (AIDS, 2001-2008) and AIDS Education Global Information System (AEGIS). Experts in the field

were contacted for recommended literature. A recently conducted systematic review was also used to identify relevant references.[6]

2.3) Study selection, data extraction and quality assessment

The citation manager, RefWorks, was used to download, remove duplicate citations and organise studies from search results. These studies were then screened by title and abstract according to the inclusion and exclusion criteria. After the first screening, the full article of all studies considered potentially eligible were retrieved and further reviewed for eligibility whereas conference abstracts were screened first by title, then by full abstract. After all potentially eligible studies were selected, relevant data were extracted and the methodological quality was examined. The "Strengthening the Reporting of Observational Studies in Epidemiology" (STROBE) statement checklist [7] was used to develop this data extraction form and quality assessment tool (Appendix 8). Only full articles were assessed for methodological quality. The following factors were addressed, depending on the type of study: clear definition of outcome variable, reliability of the measure of assessment, clear outline of the number of patients at each stage of the study, adjustment of confounders, confidence intervals and p-values presented. A study scored 1 point if the criterion was fulfilled, 0.5 points if it was partially met and 0 if it was not fulfilled. The points were then tallied and the methodological quality was rated accordingly, <50% (poor), 50-74% (average) and ≥75% (good). Barriers and facilitators were categorised according to 3 domains: psycho-social (related to a patient's attitudes and beliefs), economic (related to a patient's resources) and health systems (factors influencing service in a health facility).

3) RESULTS

3.1) Characteristics of included studies

The search yielded a total of 760 citations (Fig 3). After the first screen, 70 potentially eligible studies remained (54 articles and 16 abstracts). Twenty-five studies were excluded because they were of poor methodological quality (n=11), did not meet the inclusion criteria (n=9) and were inaccessible (n=5). Overall, 45 studies were retained for study analysis (36 articles and 9 abstracts). The majority of studies were conducted in South Africa (n=16) and the remainder were conducted across other parts of the region: Uganda (n=9), Kenya (n=5), Malawi (n=4), Mozambique (n=2), Ethiopia (n=2), Tanzania (n=2), Zambia (n=2), Rwanda (n=1), Swaziland (n=1), additionally one study was conducted in both South Africa and Zimbabwe. The methodological quality of most full text articles (n=19/36) was rated average as these studies scored between (50-70%) whereas 47% of studies (n=17/36) were of high quality scoring ≥75%. All studies provided an outcome definition, the majority used appropriate statistical tests (n=21/27) and 78% (n=21/27) adjusted for confounders. Common weaknesses noted in most studies were: no indication of how missing data was handled (n=19/27) and for a few studies, confidence intervals (n=6/27) and p-values (n=4/27) were not provided. Of the 8 studies that traced patients, all adequately described the method of follow-up except for one study [34].

3.2) The proportion of patients at each step of the HIV cascade

3.2.1) Enrolment into HIV care and completion of ART-eligibility assessment

Twenty studies examined step 1-4 of the cascade (Fig 1A-B, Table 1). The majority of studies (n=8) were conducted in South Africa with the remainder scattered across the region: Uganda (n=4), Ethiopia (n=2) and Kenya (n=2), Malawi (n=1), Mozambique (n=1), Rwanda (n=1) and Tanzania (n=1). Only four studies were of good methodological quality.

Nine studies indicated the percentage of HIV+ patients that registered at a medical facility for ongoing HIV care post-diagnosis. Enrolment into HIV care was assessed mainly via patient folder reviews and most studies did not incorporate time cut-offs in the definition of this variable. In non-selected patients enrolment into care ranged between 47%-70% yet between 42% [10, 20] -85% [14] in specific groups (i.e. home-based testers, mobile testers and female sex-workers (FSWs)). Only one

study followed-up patients who failed to enrol in HIV care and reported that 5% of all patients were deceased. [9] Two studies, which were of average quality and on non-selected patients [10, 14] based assessments on self-reports. Due to the potential risk of social desirability bias this could have inflated the enrolment estimates reported in these studies. One study scored 50% for study quality as confounders were not adjusted for which may have lead to an overestimation of the estimates reported. [8] Excluding this study would not have changed the range of enrolment to HIV care considerably.

Eleven studies reported the percentage of HIV+ patients that underwent ART eligibility assessment which was either assessed through laboratory-based CD4 count testing [15-22], and/ or WHO clinical staging [12]. One study scored 50% for study quality as investigators did not adjust for potential confounders which may have lead to an overestimation of the estimates. [11] Excluding this study would not have changed the range of ART-eligibility assessment considerably.

Eight studies investigated the proportion undergoing CD4 count testing (range: 55% within 8 weeks [18]-85% within 12 weeks [17]) and a further two studies assessed patient return for collection of CD4 count results (range: 85% within 8 weeks [18]- 35% within 12 weeks [17]).

3.2.2) Retention in pre-ART care

Five studies investigated the proportion of ART-ineligible patients who were retained in pre-ART care and three used time-cut offs (Table 2). Four of these studies were from South Africa; the fifth study was from Malawi. Majority (4/5) were of good methodological quality. Retention in pre-ART care in South African studies ranged between 42% (6 months) [22]-45% (13 months) [28]. Retention was almost 2-fold greater in those with CD4 counts between 200-350 cells/µl compared to those with CD4 counts >350 cells/µl in a HIV clinic in South Africa. [29] However, retention in pre-ART care reported in rural Malawi was the highest (59%), albeit no time-cut offs were used. [30] Only one study traced those individuals lost to follow-up (LTFU) and found that majority LTFU (35%) were deceased. [30]

3.2.3) Linkage to ART care

Seventeen studies investigated the proportion of ART-eligible patients who subsequently initiated ART (Table 3). More than two thirds of these studies were of average quality (69%). The majority (n=8) where conducted in South Africa whereas the remaining studies were from Kenya (n=2), Malawi (n=3), Uganda (n=3) and Mozambique (n=1). The median percentage of ART-eligible patients linking to ART care was 67% (IQR 58-81). Three studies included scored ≤60% for study quality as investigators did not adjust for potential confounders and thus the median percentage of

linkage (69%) is prone to bias .[13, 38-39] However, if these studies were excluded it would not have changed this median considerably. Almost half of the studies (n=9) failed to specify a time-cut off. Only one study examined linkage to ART care among children and showed that less than half of them initiated ART (40%). [38] The median time to ART initiation ranged from 22 days in rural Malawi [34] to 6.6 months in two semi-private hospitals in South Africa [21]. Of the eight studies indicating outcomes for those failing to initiate ART, death was common among these patients (3-25%).

3.3) Risk factors associated with retention or attrition at each step of the HIV cascade

3.3.1) Enrolment into HIV care and completion of ART-eligibility screening

Four studies examined enrolment into HIV care among individuals testing HIV+ with one having good methodological quality (Table 4). These studies were conducted in Kenya (n=1), Rwanda (n=1), South Africa (n=1), and Uganda (n=1). Being male, younger age, having 1-2 co-residents, being married and having a high CD4 count (>250 cells/μl) decreased the likelihood of enrolling in HIV care after testing in a study form rural Uganda. [26] Another study in FSWs found that the risk of not enrolling in care increased for individuals that were breastfeeding, had a known HIV+ sexual partner and reported condom use in the last sex act. [14]

Studies which examined predictors for CD4 count testing (n=3) [16, 18, 22] and completion (i.e. CD4 count testing and collection of this result) (n=2)[19, 29] were all conducted in South Africa and 2/4 were of good methodological quality. These showed that self-referred patients, distance from clinic (≥10 km), history of tuberculosis (TB) treatment, referral by healthcare provider for HIV testing and being male increased the likelihood for not undergoing CD4 count testing. [16, 18,22] Correlates associated with CD4 count testing and patient collection of this result were low CD4 count (351-450 cells/μl) , age (25-36 years), secondary schooling, the perception that people do not care what their CD4 count result is and a CD4 count does not matter if HIV+. [19, 29]

3.3.2) Retention in pre-ART care

Only one study, from South Africa, investigated factors associated with retention in pre-ART care among individuals not yet eligible for ART and was of good methodological quality (Table 4). This study found that male patients, individuals with high CD4 counts (> 500 cells/μl) and those between 16-25 years of age were at increased risk for non-retention in care. [28]

3.3.3) Linkage to ART care

Nine studies investigated determinants associated with failure to initiate ART among ART-eligible individuals (Table 4). Most were from South Africa (n=3) and the remainder were from Uganda (n=1), Malawi (n=2), Kenya (n=2). Only four were of good methodological quality. Common predictors for failure to initiate ART were being a man [21, 22, 35, 24], having advanced immunodeficiency [24, 32, 35, 37] and having lower levels of education [31, 34].

Advanced clinical stage (III, IV) was associated with death prior to ART initiation in a study conducted in Ethiopia which showed good methodological quality. [9]

Risk factors associated with non-linkage to ART care among ART-eligible individuals were assessed in two studies conducted in Ethiopia [9] and South Africa [36], with a methodological quality of 75% and 50% respectively. These predictors were having a less advanced clinical stage (I, II) [9] being a rural resident [9], being part of a recent cohort (2007-2008) [9], pregnancy [36] and age (< 25 years). [36]

3.4) Barriers and facilitators influencing the patient continuum of care

3.4.1) Enrolment into HIV care and completion of ART-eligibility screening

Four studies assessed barriers to enrolment into HIV care among those who tested HIV+ and were conducted in Rwanda [14], Kenya [10] and South Africa [20,41] (Table 5). Perceived good health (33%) [14], feeling healthy (40%) [10] and being unable to get time off work (41.4%) [20] were the main reasons for not enrolling into care as reported among FSWs, home-based testers and mobile testers, respectively. A study from Tanzania, with average methodological quality, showed that a structured referral system, transport vouchers, community escorts and supportive counselling facilitated patient enrolment into HIV care. [23] Most patients who underwent CD4 count testing in a study conducted in South Africa reported they failed to collect their baseline CD4 count because they had insufficient time to do so (29%) and were unable to get time off work (19%). [19]

3.4.2) Retention in pre-ART care

Only one study from Malawi, with high methodological quality, examined reasons for not being retained in pre-ART care among individuals not yet eligible for ART [30] (Table 5). The main reason (45.8%) was a psycho-social factor (HIV-related stigma). However, 20% of patients reported that they could not afford transport fees and nearly a third (31.6%) were dissatisfied with the care they received at the clinic. [30]

3.4.3) Linkage to ART care

Sixteen studies examined barriers to ART initiation and more than half (63%) had good methodological quality (Table 5). Most studies were conducted in Uganda (n=5) whereas the remainder were conducted elsewhere: South Africa (n=3), Zambia (n=2), Kenya (n=1), Mozambique (n=1), Ethiopia (n=1), Swaziland (n=1), Tanzania (n=1), and one conducted in both Zimbabwe and South Africa. Lack of knowledge on antiretrovirals (ARVs) (67.2%) [45], inability to afford transport fees (range: 20%-93%) [24, 44, 49] and shortage of staff (96.6%) [45] were the main psycho-social, economic and health systems barriers, respectively.

4) DISCUSSION

This review showed that substantial attrition occurred at each intermediate step between HIV testing and ART initiation. The first major drop-out occurred at the point of linkage from a HIV testing site to a medical facility for ongoing care. Once in care, the next loss occurred between CD4 count testing and collection of the test result. Less than half of the ART-ineligible patients were retained in pre-ART care (range: 42%-45 %) and nearly two-thirds of ART-eligible patients linked to ART care (median: 67%, IQR 58-81).

Approximately 47%-70% of patients linked to care following an HIV+ diagnosis. Failure to enter into the continuum care could result in death as indicated in a study from Ethiopia.[9] A study in the US showed that 69% of patients entered into HIV care, with most testing sites based at medical facilities.[53] This result compares with findings in Ethiopia whereby 70% of patients diagnosed HIV+ within a hospital linked to ongoing HIV care at this facility.[9] However, reports on linkage to HIV care from non-medical facilities (i.e. via home-based and mobile services) were shown to be less encouraging (42%) [10,20]. Facilitators such as a structured referral system, transport vouchers, community escorts and supportive counselling could assist in a patient's linkage as indicated in a study conducted in Tanzania whereby 68% of patients diagnosed HIV+ at a rural testing site accessed HIV care at an urban clinic. [23] A study from Uganda showed that men, younger individuals, being married, having 1-2 co-residents and those with high CD4 counts were more likely not to link to care. [26] Hence, post-test counselling should be intensified and focused at these individuals.

Patients undergoing CD4 count testing ranged from 77% within 1 month in Mozambique [13] to 63% within 6 months in South Africa [16]. Additionally, patient return for CD4 count collection varied between studies as a public sector clinic in South Africa showed a low return among patients (35% within 12 weeks of CD4 testing) [17] in comparison to two semi-private hospitals in South Africa (85% within 8 weeks) [18]. Results from a recent study show that retention between diagnosis and completion of CD4 count testing or clinical staging in this region is low (59%). [6] Findings from this

review indicate that a substantial proportion of HIV+ patients fail to initiate and complete CD4 count testing and most have little time to return to the clinic for this result. [19] Studies conducted in South Africa and Mozambique have shown that point-of-care (POC) CD4 count testing could reduce this loss as most patients can undergo this procedure and receive their result within 24 hours.[54-55] Moreover, this technology could improve retention as patients who were immediately aware of this result were more likely to be retained in wellness or ART programmes (44%) compared to those who had to make an additional clinic visit for their laboratory-based CD4 count result (33%).[54]

Less than half of the ART-ineligible patients were retained in pre-ART care. This result compares to the median proportion of pre-ART care retention (46%) reported in a recent review. [6] Pre-ART monitoring through CD4 count testing can ensure a gain in patient life-years due to timely initiation of treatment. [5] More than a third (46%) of pre-ART patients in South Africa were LTFU [22] and in Malawi death was a common outcome among those LTFU. [30] A pre-ART care model similar to that described in a recent study conducted in rural South Africa could potentially alleviate these high rates of LTFU as this study showed that patients receiving >6 months care from a counsellor-led pre-ART programme had a reduced risk for being LTFU and dying after ART initiation [56]. Male patients, individuals with high CD4 counts and those between 16-25 years of age were more likely not to be retained in pre-ART care in South Africa.[28] These findings underscore the importance of developing a pre-ART model of care that can help retain men and younger individuals as well as provide stronger post-test counselling to ensure patients are informed of the clinical benefits of pre-ART care retention. Provision of the anti-bacterial drug, Cotrimoxazole, could serve as an incentive to retain ART-ineligible patients in pre-ART care as shown in a study conducted in Kenya.[57]

The median percentage of linkage to ART care in ART-eligible patients was only 67% and delays in ART initiation were considerable. This result compares to the median percentage of retention between enrolment in ART care and ART initiation (68%) found in a recent review. [6] Even in paediatric care less than half of ART-eligible children linked to ART care.[38] This poor linkage was mainly due to the socio-economic challenges faced by caregivers which suggests that these individuals require additional support and education on caring for HIV+ children.[38] Delayed ART initiation increases the risk for mortality and morbidity.[3] Introducing POC CD4 count testing in clinics could reduce these delays as a study conducted in Mozambique showed a reduction by 26 days, from time to enrolment to ART initiation.[55] Additionally, more effective post-test counselling and referral systems could reduce delays and improve linkage. Research in South Africa showed that most deaths occurred before or during treatment readiness [35] and a low CD4 count was a predictor for death prior to ART initiation.[9] Fast-tracking of patients has been frequently recommended to reduce these deaths.[21,35] This strategy may reduce some early ART or pre-ART death, but the source of the problem lies further upstream in the cascade and hence solutions targeted at earlier steps might have greater effect.[3] The main reasons for non-linkage to ART care was lack of

knowledge about ARVs (67.2%) [45], inability to afford transport fees (range: 20%-93%) [24,44,49] and shortage of staff (96.6%) [45]. These findings allude to the need for more educational programmes on ARVs, provision of transport vouchers, decentralisation of care and task-shifting in clinics.[6, 22, 30, 56]

This review has a number of limitations. There was a high level of heterogeneity in the outcome definition of studies reviewed. Time-cut offs varied and most studies did not incorporate time cut-offs into their study design, making it challenging to compare and combine estimates. The sample size of some studies was small. [11,14,20,25,31] and most were of average quality. This review might be subject to publication bias as programs in more resource-constrained settings are less likely to be published. The majority of studies were from South Africa and thus our findings maybe more reflective of this setting. It was difficult to amalgamate data as some were focused on specific groups (i.e. FSWs [14], home-based testers [10], and mobile clinic testers [20]) and others on specific settings (i.e. semi-private hospitals [21, 35] and hospital emergency departments [11]). Most studies obtained their data from patient folders and only 2 tracked those LTFU.[24, 30] It is likely those LTFU may have accessed care elsewhere and thus this misclassification could have inflated attrition estimates. Certain findings were prone to social desirability bias as some studies were based on self-reports only.[10, 14] Some studies did not quantify respective barriers and facilitators (n=10) and thus it was difficult to compare studies. Several factors intrinsic to linkage to HIV/ART care in each country (i.e. stage of epidemic at the time of studies, the availability of ART, political commitment to ART) were not examined in this review and should be taken into account in future studies investigating linkage to HIV/ART care.

In conclusion, findings from this review shed light on the high degree of attrition occurring at all steps between HIV testing and ART initiation. The first area of attrition occurred during linkage to HIV care after diagnosis. This could be solved through introduction of referral systems, transport vouchers and community escorts. Increasing the number of patients that undergo CD4 testing and obtain their result can be improved through POC CD4 testing, more effective post-test counselling or referral systems as well as notifying patients telephonically of their result. Retention in pre-ART care was less than 50% in four out of five studies. Pre-ART care models should be tailored to the needs of those at risk for defaulting care (i.e. men and younger individuals) and should include effective post-test counselling with greater emphasis on the importance of retention in care despite a high CD4 count. Delays between enrolment in ART care and initiation of ART were considerable which underscores the need for interventions targeted at upstream stages of the cascade [3] to ensure patients present early for care and are retained throughout the continuum of care. If previous recommendations for patient health information tracking systems [6, 17], improved monitoring and evaluation tools [12] and standard definition of outcomes [6, 9, 17] are met, than future studies should examine the flow of patients from diagnosis to ART initiation for more accurate estimates of losses at each stage.

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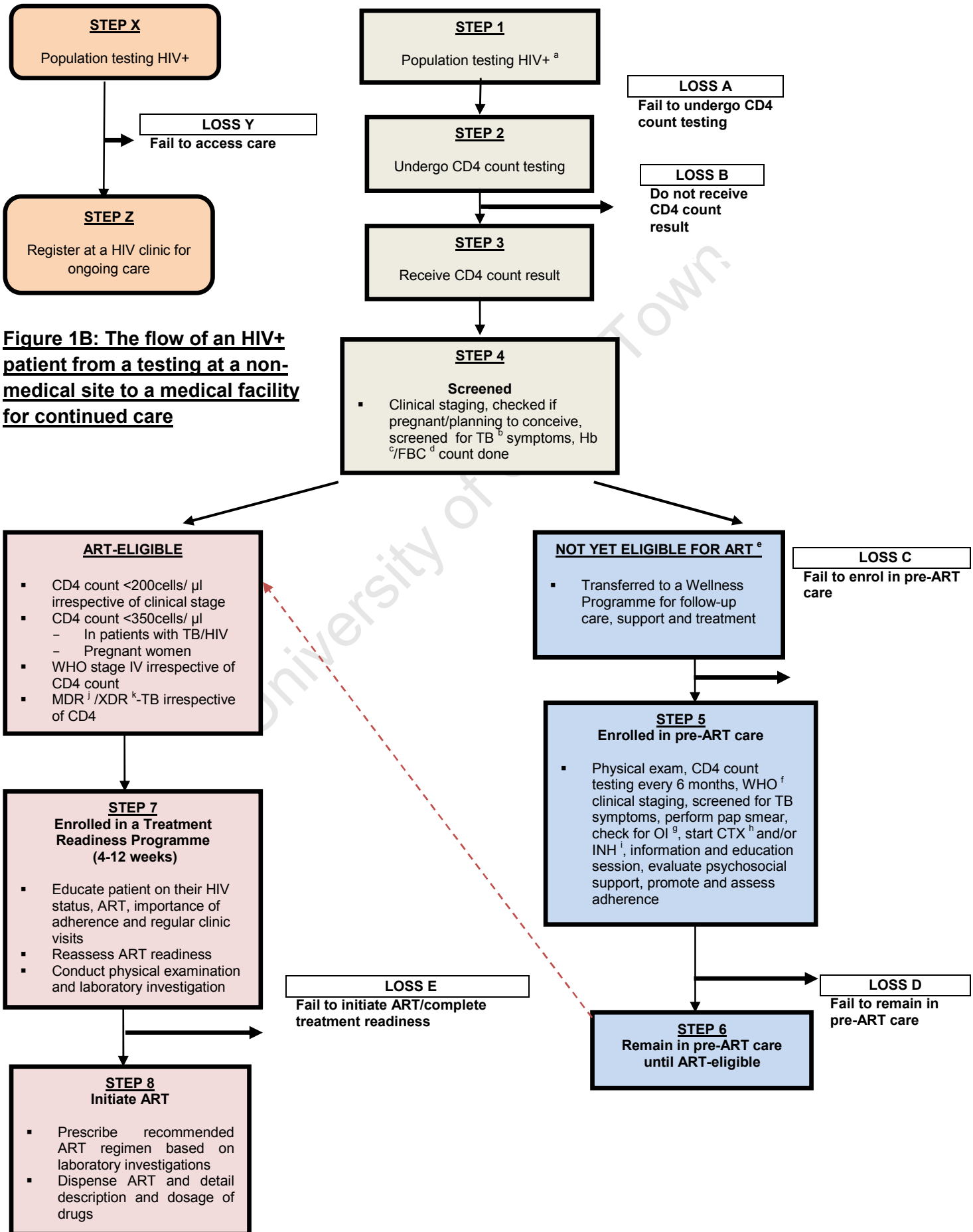

Figure 1B: The flow of an HIV+ patient from a testing at a non-medical site to a medical facility for continued care

Figure 1A: Describing each stage along the cascade from HIV testing to treatment (as per South African National guidelines) [4]

a=HIV positive, b=tuberculosis, c=haemoglobin, d=full blood count, e=antiretroviral therapy, f=World Health Organisation, g=opportunistic infections, h=Cotrimoxazole, i=Isoniazid Preventative Therapy, j=Multi-Drug Resistant, k=Extensively-Drug resistant

3		HIV
4		HIV-1
5		ACQUIRED IMMUNODEFICIENCY SYNDROME
6		Set 1-5 were combined with "or"
7	**Retention**	PATIENT DROPOUTS
8		LONG TERM CARE
9		CONTINUITY OF PATIENT CARE
10		patient dropouts
11		long term care
12		loss to follow-up
13		retention in care
14		attrition or defaulting
15		pre-art or (pre adj1 treatment) or (art adj1 initiation)
16		screening for art
17		art eligibility
18		eligible for art
19		eligibility for art
20		eligible for arv
21		art-eligible
22		Engaging
23		Engagement
24		continuum of care
25		continuity
26		Set 7-25 were combined with "or "
27		Set 6 and 26 were combined with “and”
28		Set 27 was limited to years "2000-current"
29	**Country**	DEVELOPING COUNTRY
30		AFRICA SOUTH OF THE SAHARA
31		AFRICA
32		sub-Saharan
33		*all sub-Saharan countries included as Mesh and text term combined with or*
34		Set 29-33 were combined with "or "
35		Set 28 and 34 combined with “and”
Words written in capital letters were used as MeSH headings, the others were used as free text.		

Figure 2: Detailing the compound search strategy performed on Medline and Global Health

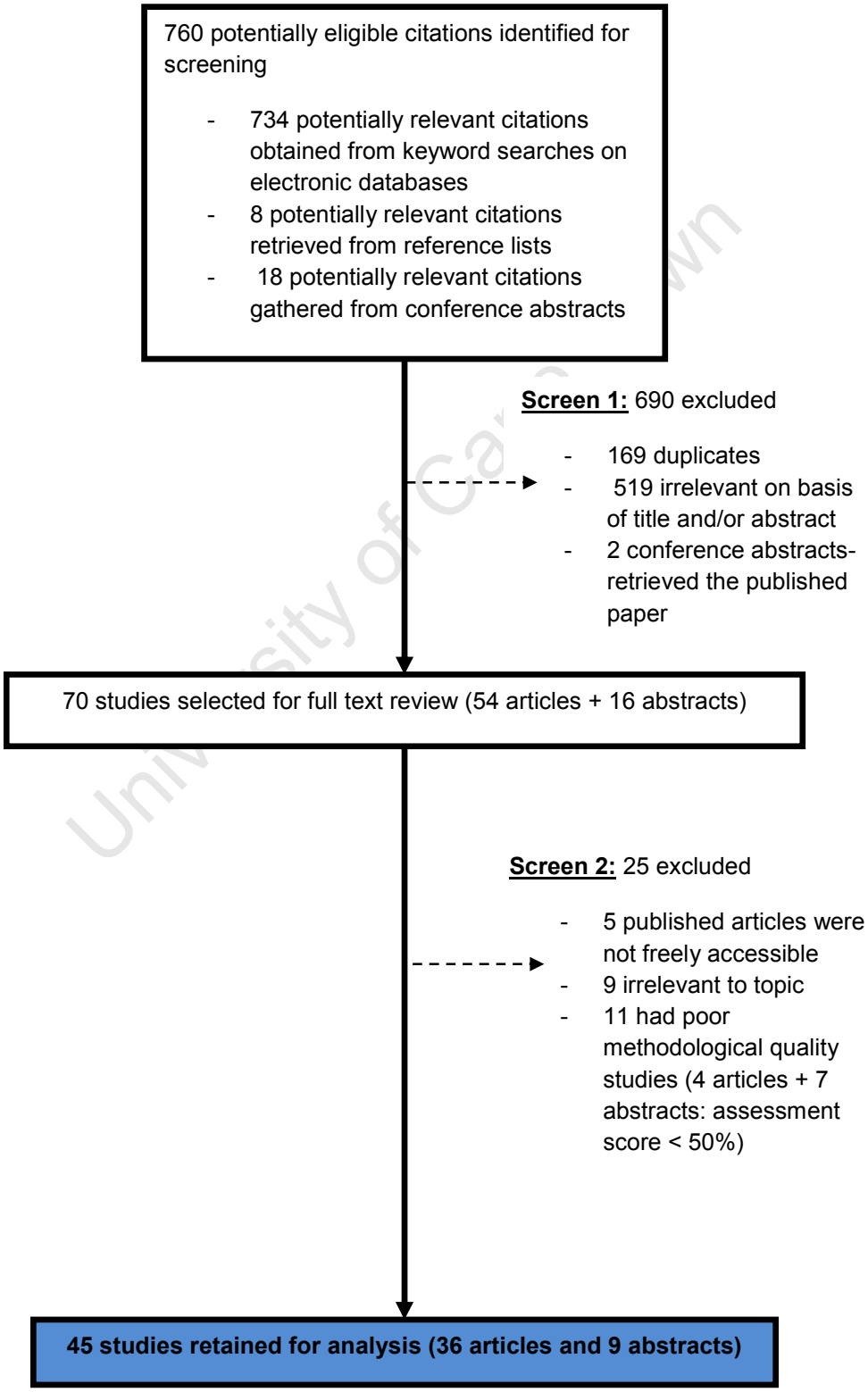

Figure 3: Diagrammatic representation of the selection process for the inclusion of studies

Table 1: Enrolment into HIV care and completion of ART eligibility assessment

Author	Country	Setting	Year of the study	Eligible (N)	Enrolled into HIV care as a prerequisite of accessing CD4 counts	Blood sample for CD4 count provided	Returned for CD4 results	Enrolled in HIV care	Quality assessment score
					(time cut-off)	(time cut-off)	(time cut-off)	(time cut-off)	
Assefa[8]	Ethiopia	Public sector sites	2008	1314				47% (immediately after testing)	50%
Assefa[8]	Ethiopia	Mobile HIV testing service for high risk individuals	2008	2035				26% (2 months)	50%
Mulissa[9]	Ethiopia	Urban, Hospital	2003-08	2191				70% (no time cut-off, but 49% enrolled the same day)	75%
Amolloh[10]	Kenya	Asembo, Home based testing service	2008-09	737				42% (2-4 months)	Abstract
Waxman[11]	Kenya	Eldoret, Emergency department, hospital	2006	61		87% (no time cut-off)			50%
Tayler Smith[12]	Malawi	Thylo, district hospital, patients with clinical stage I or II	2008-09	1428			55% (at least 1 months follow-up)		70%
Micek[13]	Mozambique	Urban, HIV testing services	2004-05	7005	57% (within 30 days)	77% (within 30 days) of those who enrolled in HIV care			60%
Braunstein[14]	Rwanda	Kigali, female sex workers	2007-08	141				85% (no time cut off)	70%
April[15]	South Africa	Cape Town, hospital, primary care clinic	2006	375		62% (within 6 months)			74%
Kranzer[16]	South Africa	Cape Town, hospital, primary care clinic	2004-09	988		63% (within 6 months)			75%
Larson[17]	South Africa	Johannesburg, hospital, clinic	2008-09	416		85% (within 12 weeks)	35% (within 12 weeks) of those who underwent CD4 count testing		70%
Losina[18]	South Africa	Durban, semi-private hospitals	2006-2007	454		55% (within 8 weeks)	85% (within 8 weeks) of those who underwent CD4 count testing		74%
Naidoo[19]	South Africa	Johannesburg, clinic		225			47% (within 1 week)		Abstract
Govindasamy[20]	South Africa	Cape Town, mobile HIV testing service	2008-09	192			73% (no time cut off), patients were notified of their result telephonically	42% (no time cut off) of those who received their CD4 result	Abstract
Bassett[21]	South Africa	Durban, semi-private hospitals	2006-08	1474		69% (within 90 days)			78%

Ingle[22]	South Africa	Free State, public sector clinics	2004-07	44844		74% (no time cut-off)			75%
Nsigaye[23]	Tanzania	Mwanza city, clinic	2005-08	349				68% (no time cut-off)	61%
Amuron[24]	Uganda	Jinja, clinic	2004-06	2483			88% (no time cut-off)		70%
Wanyenze[25]	Uganda	Kampala, hospital	2004-2005	142				56% (within 6 months)	70%
Nakigozi[26]	Uganda	Rakai community cohort study		1145				69% (6 months)	Abstract
Wanyenze[27]	Uganda	Kampala, hospital	2004	211				48% (3 months), 57% (6 months)	Abstract

Table 2: Retention in pre-ART care

Author	Country	Setting	Year of the study	Eligible (N)	Retention in pre-ART [a] care (time cut off)	Assessment of pre-ART retention	Comment	Quality assessment score
Lessells[28]	South Africa	Rural KwaZulu-Natal, public sector clinics	2007	4223	45% (13 months)	repeat CD4 count		78%
Ingle[22]	South Africa	Free State, public sector clinics	2004-07	11039	42% (6 months)	visits to the clinic	12% died, 46% loss to follow-up	75%
Larson[29]	South Africa	Johannesburg, hospital, clinic	2007-08	356	CD4 200-350: 6% within 4 months, 41% within 1 year CD4 350+: 15% within 9 months, 26% within 1 year			70%
Kranzer[16]	South Africa	Cape Town, hospital, primary care clinic	2004-09	419	46% (no time cut-off)	repeat CD4 count		75%
McGuire[30]	Malawi	Rural Malawi, district hospital, clinics	2004-07	5685	59% (no time cut-off)		4% known dead, 6% transferred out, 31% loss to follow-up (a sample of the patients lost to follow-up were traced: 26% were alive, 35% were dead, 10% moved, 29% were not found)	90%

a=antiretroviral therapy

Table 3: Linkage to ART care

Author	Country	Setting	Year of the study	Eligible (N)	Linkage to ART [a] care for those eligible (time cut off)	Median (mean) time to ART initiation	Comment	Quality assessment score
Karcher[31]	Kenya	Nyanza, district hospital	2004-05	159	78% (no time cut-off)		3% died, 13% denied treatment	65%
Tayler-Smith[32]	Kenya	Kibera slum, clinics	2005-08	2471	82% (1 month)			70%
Tayler-Smith[12]	Malawi	Thyolo, district hospital, patients with WHO [b] stage 1/2 and CD4<250 cells/uL	2008-09	681	64% (6 months)	33 days (21-44)		70%
Zachariah[33]	Malawi	Thyolo, district hospital, TB [c] patients	2003-04	742	14% (no time cut-off)			65%
McGrath[34]	Malawi	Karango, rural, district hospital	2005-06	659	86% (no time cut off)	22 days (12-29)	5% died, 0.5% had moved, 3% alive not taking ART, 5% untraceable	78%
Micek[13]	Mozambique	Urban, HIV testing services	2004-05	1506	50% (6 months)	71 days		60%
Kranzer[16]	South Africa	Cape Town, hospital, primary care clinic	2004-09	219	67% (within 6 months)			75%
Ingle[22]	South Africa	Free State, public sector clinics, eligible at first CD4 measurement	2004-07	19089	59% (no time cut off)	95 days (53-170)	25% died, 3% in care, 13% not in care	75%
Ingle[22]	South Africa	Free State, public sector clinics, eligible at subsequent CD4 measurement	2004-07	2994	58% (no time cut off)		13% died, 19% in care, 9% not in care	75%
April[15]	South Africa	Cape Town, hospital, primary care clinic	2006	72	68% (no time cut off)			74%
Bassett[35]	South Africa	Durban, semi-private hospitals	2006	501	81% (3 months)		6% died, 3% accessed a different service, 0.6% moved away, 0.6% promised to return, 6% untraceable	81%
Bassett[21]	South Africa	Durban, semi-private hospitals	2006-08	538	39% (12 months)	6.6 months	17% died	78%
Kaplan[36]	South Africa	Cape Town, primary care clinic, women	2002-07	2131	81% (no time cut off)		4% died, 7% loss to follow-up	50%
Lawn[37]	South Africa	Cape Town, primary care clinic	2002-05	1235	75% (no time cut off)	34 days (28-50)	5% died, 9% preparing for ART, 11% loss to follow-up	72%
Feucht[38]	South Africa	Pretoria, urban, hospital, children	2004	243	40% (no time cut off)			50%
Geng[39]	Uganda	Mbarara, clinic	2009-10	697	58% (3 months)			53%
Amuron[24]	Uganda	Jinja, clinic	2004-06	2182	85% (no time cut- off)	33 days (15-406)	Survival status was investigated for all losses between testing and treatment (included losses of patients not returning for their CD4 result): 7% died, 8% on ART with a different provider, 6% were alive and not on ART, 4% untraceable	70%

Parkes[40]	Uganda	NGOs [d] and governmental health units	2004-06	458	61% (3 months)			Abstract

a=antiretroviral therapy, b= World Health Organisation c=tuberculosis, d=non-governmental organisations

Table 4: Factors influencing the patient continuum of HIV care

Author	Country	Setting	Year of the study	Eligible (N)	RISK FACTORS							Quality assessment score*
					Not enrolling in HIV care*	Not having a timely CD4 count*	Completing CD4 count testing*	Not retaining in pre-ART [a] care*	Not initiating ART*	Death prior to ART initiation*	Non-linkage to ART care	
Mulissa[9]	Ethiopia	Urban, Hospital	2003-08	2191						Enrolled in an early phase (January 2003-August 2006), advanced WHO [b] stage (III, IV)	Less advanced WHO stage (I, II), rural resident, part of a recent cohort (September 2007-December 2008)	75%
Amolloh[10]	Kenya	Asembo, Home based testing service	2008-09	737	**Enrolling in care** Older age, female, HIV disclosure, perceived poor health, testing as a couple/family, having another household member enrolled in care							Abstract
Karcher[31]	Kenya	Nyanza, district hospital	2004-05	159					**Treatment denial** Pregnancy, lower level education			65%
Tayler-Smith[32]	Kenya	Kibera slum, clinics	2005-08	2471					Age (<35 years), severe malnutrition, active pulmonary TB [c], severe bacterial infection and prolonged unexplained fever			70%
Braunstein[14]	Rwanda	Kigali, female sex workers	2007-08	141	Breastfeeding, known HIV+ [d] sexual partner, reported condom use in the last sex act							70%

Kranzer[16]	South Africa	Cape Town, hospital, primary care clinic	2004-09	988		Self-referred patients **Having a CD4 count done** Diagnosed in an earlier calendar period (TB clients, 2007-2009)		**Having a repeat CD4 count** Age (≥ 30 years, VCT [e] clients)				75%
Larson[29]	South Africa	Johannesburg, hospital, clinic	2008-09	416			Low baseline CD4 count (351-450 cells/μl), employed					70%
Losina[18]	South Africa	Durban, semi-private hospital	2006-2007	454		Distance from clinic (≥10 km), history of TB treatment, referred by healthcare provider for HIV testing						74%
Naidoo[19]	South Africa	Johannesburg, clinic		225			**CD4 count collection** Age (25-36 years), secondary schooling, perception that people do not care what their CD4 count result is, CD4 count does not matter if you are HIV+					Abstract
Govindasamy[20]	South Africa	Cape Town, mobile HIV testing service	2008-09	192	**Enrolling into care** Low CD4 count (≤350 cells/μl), disclosure, presence of TB symptoms, unemployment		**Receiving result telephonically** Low CD4 count (≤350 cells/μl), being female, the availability of a phone number					Abstract
Bassett[21]	South Africa	Durban, semi-private hospitals	2006-08	1474					Men, patients with no family/friends who were HIV-infected			78%
Ingle[22]	South Africa	Free State, public sector clinics	2004-07	44844		**No recorded pre-**			Men, enrolled in a rural clinic, clinic with low staffing levels,			75%

						treatment CD4 count Male, enrolled in 2007, no national ID [f] number			distance from clinic			
Bassett[35]	South Africa	Durban, semi-private hospitals	2006	501					Male, unemployed, baseline CD4< 100 cells/µl			81%
Kaplan[36]	South Africa	Cape Town, primary care clinic, women	2002-07	2131							Pregnancy, age (< 25 years)	50%
Lawn[37]	South Africa	Cape Town, primary care clinic	2002-05	1235					Advanced immunodeficiency			72%
Lessells[28]	South Africa	Rural KwaZulu-Natal, public sector clinics	2007	4223				High CD4 count (> 500 cells/µl), male, young age (16-25 years)				78%
Nakigozi[26]	Uganda	Rakai community cohort study		1145	Male, younger age (15-24 years), having 1-2 co-residents, married, CD4> 250 cells/µl							Abstract
Amuron[24]	Uganda	Jinja, clinic	2004-06	2182					**Incomplete screening** Male, low CD4 count (<50 cells per 10^6/l)			70%
McGrath[34]	Malawi	Karango, rural, district hospital	2005-06	659					Less education, difficulty dressing, more delayed ART initiation appointment, mid-upper arm circumference < 22 cm			78%
Zachariah[33]	Malawi	Thyolo, district hospital, TB patients	2003-04	742					**Non-acceptance to ART** Cost of transport to ART site			65%

*= as per sub-heading unless otherwise stated
a=antiretroviral therapy, b= World Health Organisation, c=tuberculosis, d=HIV positive, e=voluntary counselling and testing, f=identification

Table 5: Barriers and facilitators impacting on the HIV testing to treatment cascade

thor	Country	Setting	Barriers and/or Facilitators of:	BARRIERS[$]				FACILITATORS		Quality assessment score
				Psycho-social	Economic	Health Systems	Other	Health System	Organisational	
Braunstein [14]	Rwanda	Urban-Kigili, VCT [a] clinic. FSWs [b]	Enrolment into HIV care	Perceived good health (33.3%) High CD4 count at diagnosis* Belief that care was unnecessary*						70%
Nsigaye[23]	Tanzania	Mwanza city, clinic	Enrolment into HIV care					Transport voucher* Community escort*	Supportive counselling* Structured referral system*	61%
Amolloh[10]	Kenya	Rural, HBC [c] patients	Enrolment into HIV care	Still felt healthy (44%) Did not believe HIV test result (22%) Confidentiality or stigma concerns (20%)						Abstract
Govindasamy [20]	South Africa	Cape Town, mobile HIV testing service	Enrolment into HIV care	Fear toxicity and side-effects of ART (12.6%) Fear of disclosure of one's HIV+ status/stigma associated with being HIV+ /social isolation (8.8%)	Work during the day and cannot get time off (41.4%) Clinic too far away from work (15.7%)					
Luseno[41]	South Africa	HIV clinic, randomised community trial, high risk women	Enrolling into HIV care	HIV-related stigma and discrimination*		Long waiting time* Low quality care* Judgemental and unresponsive staff*				Abstract
Naidoo[19]	South Africa	Peri-urban, Primary healthcare clinic-Johannesburg	Collection of CD4 count	Insufficient time to return to the clinic for result (29%)	Difficult to get time off work (19.6%) Difficulty with transport costs and distance to the clinic (7.4%)					Abstract
McGuire[30]	Malawi	Rural, ART [d] clinic	Retention in pre-ART care *Followed-up those LTFU [e]	HIV-related stigma (45.8%) Perception of health improvement (28.9%) Lack of support by partner (13.9%) Opting for traditional medicine (9.2%) Poor health (4.6%) Fear drug toxicities (1.3%)	Cannot afford transport costs (20.1%)	Dissatisfied with care/staff behaviour (31.6%) Inconvenient clinic hours (5.9%) Long waiting times (3.3%)				90%

Posse[42]	Mozambique	Rural and urban, ART clinic	ART initiation		Patient resources# <40% Transport costs Distance from home to the health facility Food resources	Shortage of HCWs [f] # 45% Long waiting time for CD4 count result # 45% Lack of community information # 47%				85%
Lubega[43]	Uganda	Peri-urban, Iganaga, pre-ARV [g] clinic	ART initiation	Fear of being beaten or divorced by one's husband* Lack of incentives to seek pre-ART care*	Cannot afford transport costs*	High staff workload * Inadequate post-test counselling* Competition with traditional healers* Long waiting times*				100%
Duff[44]	Uganda	Rural and urban-Kabarole, PMTCT [h] clinic	ART initiation	Perceived that ART should be commenced when bedridden (60%) Non-disclosure of HIV+ [i] status (18.9%) HIV-related stigma*	Costly transport fees (93%)	Negative patient-provider interactions (33%) Long waiting times* Staff favouritism of patients*				85%
Kunihira[45]	Uganda	Rural-Rakai, ART clinic	ART initiation	Lack of knowledge on ARVs (67.2%) Fear to be seen at the clinic (66.1%) Do not know if it is HIV/AIDs-think they are bewitched (17.2%) Fear side-effects of drugs (19.3%)	Long distance to treatment centres (50.5%) Lack of food (24.5%) Not aware of free-ARVs (18.8%)	Shortage of staff (96.6%) Long waiting times (52.9%)				80%
Amuron[24]	Uganda	Rural and semi-urban, ART clinic	ART initiation	Not ready to start ART (7%) Experiences difficulty in disclosing HIV status (4%) Requested to be referred to a clinic nearer ones home but failed to turn up for treatment (4%) Wants to complete TB [j] treatment before starting ART (3%) Fear toxicity and side-effects of ART (1%) Failed to identify a treatment buddy and did not return to the clinic (1%)	Cannot afford transport costs (44%)					70%
Parkes[40]	Uganda	Rural, NGO [k] health units	ART initiation	Medically unfit (10.5%) Uncertain about which service provider to choose (10.0%) Difficulties in understanding (6.7%) Domestic problems (6.7%)	Transport or Financial constraints (7.7%) Relocating (7.7%)	Awaiting ART team home visit (10.6%) Administration issues (3.9%)	Initial phase of TB treatment (8.9%)			Abstract

Mshana[46]	Tanzania	Rural, VCT clinic	ART initiation	HIV-related stigma* Reluctant to identify a treatment buddy*	Cannot afford transport and food costs*	Confusing hospital set-up* Low drug supply* Unfriendly HCWs*		Transport voucher*	Facilitated at hospital*	80%
Fox[47]	Zambia	Rural and urban: Southern, central and Lusaka Province, patients on ART & HBC (patients who did not initiate ART)	ART initiation	HBC patients: HIV-related stigma (54%) Don't have time to get to the clinic (1.0%)+, (4.6%)++	The clinic is too far to travel to (27.4%)+, (41.3%)++ Difficult to get to the clinic (17%)+, (21.6%)++ Can't leave work to get to the clinic (13.8%)+, (6.9%)++ Have to/may have to: Pay to travel to the clinic (48.2%)+, (14.7%)++ Visit the clinic more than once a month (31.2%)+, (26.3%)++ Pay someone to take over tasks (13.5%)+, (2.5%)++ Pay a fee at the clinic (9.5%)+, (4.5%)++ Accrue other costs (12.0%)+, (13.6%)++ Spend the night away from home (0.7%)+, (2.0%)++	Convenience of clinic hours ^ (77%)+, (66.3%)++ Counselling ^ (56.0%)+, (73.5%)++ Provider time ^ (45.5%)+, (75%)++ Service ^ (40.5%)+, (85%)++ Staff concern ^ (37%)+, (74%)++ Waiting time ^ (17.6%)+, (22.5%)++				85%
Murray[48]	Zambia	Urban women, Lusaka	ART initiation	Consider ART to be bad (93.6%) Fear side effects and stigma (70.2%) Do not know much about HIV (46.8%) Scared of ending marriage (31.9%) Failure to accept status (23.5%)	Need food (17.0%)					83%

Nunu[49]	Swaziland	Rural, public sector hospitals	ART initiation	Non-disclosure to partner (6.7%)	Cannot afford transport costs (20%) Difficulty to get time off work (13%)	Laboratory system failure*	Admitted to hospital (6.7%) On TB treatment* Late arrival to clinic*			Abstract
Unge[50]	Kenya	Urban township, Kibera	ART initiation	Fear of taking medication on an empty stomach* Fear side-effects of medication* Fear disclosure and possible repercussions* Concern for continuity of care and treatment* Seeking alternate care* Conflicting information from religious/community leaders*	Lack of food*					83%
Assefa[8]	Ethiopia	Rural and urban, public sector sites	ART initiation	HIV-related stigma* Perceived good health* Opting for traditional medicine* Fear side-effects of drugs*	Cannot afford transport fees* Long distance to the health facility*	Inadequate post-test counselling*				50%
Clouse[51]	Zimbabwe and South Africa	Semi-urban and rural, HIV clinic	ART initiation	Employment commitments*	Cannot afford transports fees* Relocated*					75%
Bassett[35]	South Africa	Urban and peri-urban, semi-private hospitals	ART initiation	Feeling unready to commence ART (1.2%)	Changed service provider (18.3%) Relocated (3.7%)					81%
Feucht[38]	South Africa	Urban, Paediatric ART clinic	ART initiation	Social problems (17.3%): (Caregiver's refusal to disclose HIV status to another adult, denial of child's status/ill health/need for ART. Caregiver's substance abuse)	Referral to other ART site (3.0%)	Lack of human resources (20.3%) Incorrect disease stage classification (13.7%)	Co-infected with TB (26.4%) Acute illness (2.5%) Current stable medical condition (10.7%)			50%
Bianchi[52]	South Africa	Primary healthcare clinics, ART clinic	ART initiation		Unable to take time off work (54%)					Abstract

$= percentages may not add up as reasons such as "no reason", "other", "patient refused" were not presented, *=percentage not reported, #= Patients were asked to score each factor. Factors scoring <50% were regarded as barriers.
+=HBC urban patients, ++=HBC rural patients, ^= patient's rating of each factor
a=voluntary counselling and testing, b=female sex workers, c=home-based care, d=antiretroviral therapy, e=lost to follow-up, f=healthcare worker, g=antiretrovirals, h=prevention of mother to child transmission, i=HIV positive, j=tuberculosis, k=non-governmental organisations

PART C: ARTICLE

Linkage to HIV Care from a Mobile Testing Unit in South Africa by Different CD4 Count Strata

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PART C: ARTICLE

Linkage to HIV Care from a Mobile Testing Unit in South Africa by Different CD4 Count Strata

RUNNING HEAD

Linkage to HIV care from a Mobile Testing Unit

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CONFLICT OF INTEREST

None to declare

ABSTRACT

Background

The linkage and barriers of linkage to facility-based HIV care from a mobile HIV testing unit have not previously been described.

Methods

A stratified random sample (N=192) was drawn of all eligible, newly-diagnosed HIV-infected individuals with a laboratory CD4 count result on a mobile unit between August 2008 and December 2009. All individuals with CD4 counts ≤ 350 cells/μl and 30% of individuals with CD4 counts > 350 cells/μl were sampled. Linkage to care was assessed during April to June 2010 in those that received their CD4 count result. A participant who accessed HIV care at least once after testing was regarded as having linked to care. Binomial regression models were used to identify clinical and socio-demographic factors associated with receiving a CD4 count result and linking to care.

Results

Forty-three (27%) individuals did not receive their CD4 count result. A lower CD4 count, being female and the availability of a phone number increased the likelihood of receiving this result. Follow-up was attempted in the remaining 145 individuals. Ten refused to participate and contact was unsuccessful in 42.4%. Linkage was 100% in patients with CD4 counts ≤ 200 cells/μl, 66.7% in individuals with CD4 counts of 201-350 cells/μl and 36.4% in those with CD4 counts > 350 cells/μl. A lower CD4 count, disclosure, presence of TB symptoms and unemployment increased the likelihood of linking to care.

Conclusion

Linkage to care was best among those eligible for ART. Interventions designed at improving linkage among employed individuals are urgently warranted.

Key Words

Mobile HIV testing unit, linkage to HIV and ART care, barriers to linkage to HIV care.

INTRODUCTION

In 2008 an estimated 1.9 million deaths were attributable to HIV/AIDS in Sub-Saharan Africa. [1] HIV-infected individuals from this region usually present for care late and thus commence antiretroviral therapy (ART) with advanced immunodeficiency thereby increasing their risk for HIV-related mortality. [2-7]. HIV testing remains the entry point to a continuum of HIV medical care and social support. [1] Over the past few years the number of HIV testing sites has been scaled-up significantly. [1] However, increasing testing is of little use without strategies to direct newly-diagnosed HIV positive (HIV+) patients to appropriate packages of HIV care.

There is a dearth of published literature on retention in ART programmes yet few studies have examined linkage to HIV care. Nonetheless, recent studies have shown that linkage to care from traditional HIV testing points at stationary facilities is often inadequate and varies across sites. [8-13] Factors known to enhance enrolment to care at these sites include use of referral forms, transportation allowances and community escorts. [12] The main predictors of non-linkage to HIV and ART care from these facilities include unemployment [8], user-fees [8], distance of clinic [10,12], transport costs [12], lack of education [14], history of tuberculosis (TB) treatment [10], referral by healthcare providers [10] as well as being male [11], a young adult [11] or a TB patient [11]. Noteworthy is that failure to access care is prominent among those with lower CD4 counts [8] and individuals self-referred for testing. [11] Successful interventions resulting in earlier diagnosis of HIV must also be accompanied by strategies that enhance linkage into HIV care in order to improve health outcomes.

Mobile HIV testing services have been shown to facilitate testing of individuals earlier in their stage of HIV infection and to be more accessible to hard-to-reach and high-risk populations. [15-19] Moreover, streamlined HIV counselling and testing (HCT) procedures offered by mobile services allow for a high number of individuals to be screened. [15-19] Evidence indicates that in comparison to stationary testing facilities, mobile testing units are cost-effective in diagnosing new cases of HIV. [19] However, ongoing HIV care may not be sustainable from mobile units therefore requiring patients to be referred to stationary facilities for the necessary follow-up care. Furthermore, it is possible that linkage to facility based care from these units is inadequate because of their mobile nature. [12]

To date, no study has assessed the extent to which people diagnosed with HIV in mobile testing units' link to HIV medical care at public healthcare facilities. Understanding the associated challenges of linkage to HIV care from mobile units is important if this mobile approach is to be considered for the expansion of HCT. The aim of this study was to assess the proportion and characteristics of individuals who accessed HIV care after testing HIV+ in a mobile testing unit and to describe the barriers of linkage to care.

METHODS

Study Design

Individuals diagnosed with HIV (for the first time) at the mobile unit during a 16 month period were identified retrospectively through mobile unit records. Those who received their laboratory CD4 count result were prospectively followed up to assess linkage to HIV care.

Setting and population

A nurse-run and counsellor-supported mobile testing unit, as described elsewhere [15], provided free HCT services to underserved communities within the Cape Metropolitan region, Western Cape, South Africa.

Client-initiated HCT was offered in combination with free screening for other chronic conditions (i.e. hypertension, diabetes and obesity) and TB to a predominantly black Xhosa-speaking African population. HCT was performed according to the Provincial Government guidelines. [20] Individuals who consented to rapid HIV testing and tested positive were subsequently clinically staged and underwent laboratory CD4 count testing.

After the completion of testing, individuals received a referral letter to take to a healthcare provider to facilitate their access to HIV care. Nurses detailed all conditions that the individual was referred for on this letter (i.e. HIV/ART care, concomitant medical problems and/or screening for other conditions). When CD4 counts became available (usually within 72 hours) patients were contacted telephonically and received their results. If contact numbers were unavailable, home visits were done or a letter was sent to the patient, requesting the individual to contact the counsellor for their result. Once contact was established, the CD4 count result was received and implications discussed. All HIV+ patients were encouraged to attend clinics for either HIV care or to start ART if eligible according to South African national guidelines [21] and other non HIV-related health services if necessary. The aforementioned procedures were followed for all HIV+ patients.

Sampling strategy

Records of all those who were newly-diagnosed with HIV between August 2008 and December 2009 were accessed and reviewed to identify an eligible cohort (Fig.1). Only those had a laboratory CD4 count done were eligible for follow-up. The majority of newly-diagnosed HIV+ individuals diagnosed on this mobile unit have CD4 counts > 350 cells/μl. [15] Due to a higher proportion of patients in this stratum a stratified random sample was drawn. A 100% of individuals with laboratory CD4 counts ≤ 350 and 30% of individuals with laboratory CD4 counts > 350 cells/μl were sampled.

Protocol deviation

The calculated sample size in the protocol (n=225) was an overestimation as the predicted number of eligible patients for December 2009 was high, it included those patients that received their CD4 count result via post and it was based only on electronic patient data that needed further cleaning. (See Appendix 11)

Follow-up for assessment of linkage to HIV care

Eligible individuals who had previously received their CD4 count result were telephoned or interviewed in person between April and June 2010, to obtain informed consent (Fig. 2). At least 3 telephonic attempts were made to track the participant and if no contact number was available a home visit was conducted. A questionnaire was subsequently administered to those consenting to participate.

Verification of self-reported linkage to HIV care

A clinic folder review was conducted at respective public healthcare facilities on participants who reported they linked to medical care, once additional consent was acquired for this process (Fig.2).

Ethics

Informed consent (written or verbal) was obtained from participants. Data collection and analysis was approved by the University of Cape Town Research Ethics Committee and the Provincial Government of the Western Cape Research Ethics committee.

Outcome definitions (See appendix 14 for predictor definitions)

Outcomes:

Laboratory CD4 count result received: A newly-diagnosed HIV+ individual who tested at the mobile unit and was subsequently successfully contacted (telephonically or by home visit) and received their laboratory CD4 count test result.

Linked to care: A newly-diagnosed HIV+ individual who accessed HIV care at a public healthcare facility at least once after testing on the mobile unit.

Statistical analysis

Data were double entered into EpiData Entry (Version 3.1) and analysis was carried out using STATA (Version 11.0, Stata Corporation. LP, College Station, TX, USA). Data were first explored via cross-tabulations and chi square tests. Total proportions were calculated taking sampling weights into account. Baseline characteristics of the stratified random sample (N=192) were used to identify correlates of receiving a laboratory CD4 count result through a binomial regression. Variables that had 10% significance in the bivariate analysis were included in the multivariate model. In addition, clinical and socio-demographic variables of all participants (N=77) were examined to ascertain those that best predicted linkage to care through a binomial regression, using bivariate analysis only. All variables in the regression analysis were controlled for laboratory CD4 count strata.

RESULTS

A total of 6738 records of individuals accessing the mobile service (51.2% female) between August 2008 and December 2009 were available (Fig.1). The overall prevalence of those newly-diagnosed with HIV was 6.9% (463/6738). Only 376 (81.2%) of these patients met the study's inclusion criteria. A stratified random sample (N=192) was then drawn from this cohort (N=376): 36/36 individuals with CD4 counts ≤ 200 cells/µl, 80/80 individuals with CD4 counts between 201-350 cells/µl and 30% of individuals with CD4 counts > 350 cells/µl (76/260) were sampled.

Baseline characteristics of individuals in the stratified random sample

Of the 192 patients sampled, the majority was women (60.5%) and the mean age was 34.8 years (Table 1). In total, 60.2% had tested for HIV previously. The mean CD4 count was 488.6 cells/µl, majority (60.4%) was in WHO clinical stage I and the mean body mass index (BMI) was 26.7 kg/m^2. Furthermore, TB symptoms occurred in 20.7% and 81.8% of individuals had access to a cellphone.

Baseline characteristics of individuals who received a CD4 count result and those that did not

There were slightly more females in the group that received their CD4 count result (63.7% vs.52.8%) (Appendix 13). The proportion that had access to a cellphone was almost 40% higher in those that received their CD4 count result (94.8% vs. 51.5%) The median age in both groups was roughly similar (35.2 years vs. 33.9 years). The median CD4 count result among those that received their result was slightly lower (456.4 cells/µl vs. 563.9 cells/µl).Less than a third of individuals in each group had TB symptoms (20.0% vs. 22.4%).

Predictors for receiving a laboratory CD4 count result

A total of 73% of individuals received their CD4 count (Table 1). Receipt of a CD4 count result was 0.82 times less likely for individuals with CD4 counts > 350 cells/µl compared to individuals with CD4 counts ≤ 350 cells/µl (95% CI: 0.69-0.98) (Table 2). Being a woman, having access to a cellphone and having lower CD4 counts were factors that increased the likelihood of receiving CD4 count results in the bivariate analysis. Results were similar in the multivariate analysis: individuals with a CD4 count > 350 cells/µl were 0.85 times less likely to receive their CD4 count result (95% CI: 0.73-0.99). Availability of a cellphone made a successful contact twice as likely.

Baseline characteristics of individuals lost to follow-up

Of the 145 individuals eligible for follow-up, 56 (42.4%) were untraceable (Fig.1). This included 13 with CD4 counts < 200 cells/μl (46.4%), 20 with CD4 counts in the mid range (32.3%) and 23 with CD4 counts > 350 cells/μl (51.1%). The majority were women (52.9%) with a mean age of 34.2 years, mean BMI of 26.5 kg/m^2, mean CD4 count of 458.3 cells/μl and were in WHO clinical stage I. Moreover, TB symptoms were prevalent in 16% and most (95.1%) had access to a cellphone.

Characteristics of study participants

Seventy-seven newly-diagnosed HIV+ patients participated (Table 3). Most of these individuals completed primary school (84.8%). Unemployment was more prevalent in individuals with CD4 counts ≤ 200 cells/μl (76.9%) compared to individuals with CD4 counts >350 cells/μl. Of the 69.3% who disclosed their HIV status, only a small proportion (10.9%) felt stigmatised after disclosing. The majority of participants (73.8%) rated their health status as “strong”.

Linkage to HIV care

Overall, 52.5% (49) accessed HIV medical care (Table 3). There was an inverse relationship between CD4 count result and linkage to care: all of those with CD4 counts ≤ 200 cells/μl linked to care, however, 66.7% and 36.4% of those with CD4 counts between 201-350 cells/μl and > 350 cells/μl, respectively, linked to care. The overall mean time from diagnosis to accessing HIV care was 2.2 months. Those with CD4 counts ≤ 200 cells/μl took on average less than a month (3 weeks) to access care whereas those with CD4 counts > 350 cells/μl took a mean time of 3 months. Of those with CD4 counts ≤ 200 cells/μl 69.2% started ART within 2 months of diagnosis and the remaining 30.8% were within the ART screening process.

Verification of self-reported linkage to HIV care

Among the 49 who linked to care, 43 (88%) provided additional consent to access their clinic folders. Eight (19%) of these folders were untraceable. A validation of the 35 (81.4%) clinic folders which were traced showed that the sensitivity of self-reported linkage to care was excellent (100%).

Predictors of accessing HIV medical care

Those contactable patients with CD4 counts > 350 cells/μl were 0.49 times less likely to link to care compared to individuals with CD4 counts ≤ 350 cells/μl (95% CI: 0.27-0.87) (Table 4). In the bivariate analysis, individuals who had TB symptoms and who had disclosed their HIV status were more likely to link to care whereas those employed were less likely.

Barriers of linking to HIV care

The most common stated barrier (41.4%) to linking to care was the inability to access public healthcare facilities during working hours and many participants reported that they could not get time off work (Table 3).

DISCUSSION

Losses can occur at critical phases in the cascade from HIV testing to care. This study highlights the challenges of contacting newly-diagnosed HIV+ individuals accessing a mobile testing service in order to inform them of their CD4 count result and the poor linkage to HIV care among those with higher CD4 counts. Results also indicate that linkage to care among those eligible for ART from this mobile unit is higher than that reported in studies examining linkage from stationary facilities.

Approximately 27% of newly-diagnosed HIV+ individuals did not receive their CD4 count result. This could result in delays in entering into HIV care. Findings indicate that a CD4 count result of ≤ 350 cells/μl, availability of a cellphone and being female increased one's likelihood for receiving a CD4 count result. Other recently conducted studies in South Africa have shown poor return for CD4 count results particularly in patients with higher CD4 counts. [9, 10] In this study, the CD4 count variable was adjusted for in the model as it is conceivable that due to the urgency for ART-eligible patients to link to care, personnel may have placed more emphasis on following up this stratum of patients with their result, despite protocol, additionally, these patients may have felt unwell at the time of diagnosis therefore might have actively facilitated the receipt of their result. Overall, these data underscore the difficulties faced in following up clients after blood is drawn for laboratory CD4 testing and the value of point-of-care (POC) CD4 count testing on mobile units and stationary facilities to attenuate the high attrition occurring between HIV diagnoses and receiving a CD4 count result.

In this study linkage to care among the ART-eligible patients who could be traced was 100%, albeit a small sample size. This finding was unexpectedly higher than studies assessing linkage to care in stationary facilities as these found a 30-80% linkage among ART-eligible individuals. [8-13]

This study showed that there was a delay from time of diagnosis to initiation of ART in that 30.8% of these individuals were still waiting to commence ART after 2 months post diagnosis. This period of ART initiation delay is consistent with findings from South Africa (3-6 months) [8-11], Mozambique (3 months) [13] and Malawi (22 days after screening) [14]. This indicates the need for further interventions, if recommendations of shortening treatment readiness programmes and prioritising those with advance disease are met. [8] In contrast, this study found that linkage to care among those with higher CD4 counts was poor as more than 60% of those with CD4 counts > 350 cells/μl failed to access care. This is similar to the findings from two South African studies conducted in stationary services [9, 11]; however there is a paucity of studies assessing linkage to care among ART-ineligible patients. More data and possibly better interventions in this category are required as test and treat strategies are contemplated for reducing population HIV transmission.

These results also illustrate that having a higher CD4 count, no TB symptoms, not disclosing an HIV+ status and being employed increased one's risk for not linking to care. Patients who are physically well may not perceive the need to register for follow-up care, especially those in the higher CD4 count bracket. Hence linkage to care at healthcare facilities maybe considerably higher than mobile services because patients presenting at these sites have advanced disease compared to those accessing mobile services. [15] Those patients with lower CD4 counts and TB symptoms were possibly more motivated to link to care because of their weakened physical condition at time of diagnosis or mobile unit staff may have put greater emphasis on the urgency to link to care based on their clinical results. Unemployment was the highest among individuals with CD4 counts ≤ 200 cells/μl hence these individuals may have had time during the day to access clinics.

The fact that clinics are inaccessible outside working hours was identified as a major barrier to linkage to care from a mobile unit. The mobile unit, unlike state run facilities operates outside of traditional working hours and hence may have accessed clients who would not have tested due to difficulties with clinic operating hours. It is likely that those who access the mobile unit outside working hours and on weekends have difficulty in subsequently linking to care at a public healthcare facility. Thus, extending service hours to evenings and weekends at public clinics and establishing work-place programmes through mobile units might improve linkage to care among the working population. This study would suggest that at least adequate advice and support on disclosure of an HIV+ status might improve linkage to HIV wellness programmes.

These study findings are subject to several limitations. The small sample size limited the power to detect associations particularly in the group of individuals with CD4 counts ≤ 200 cells/μl. Notably

42.4% of patients were untraceable despite multiple follow-up attempts which might have resulted in a biased estimate. The strata with < 200 and > 350 CD4 cells/μl had the greatest proportion of uncontactable patients. Follow-up of HIV+ patients was challenging as this study was conducted 6-18 months post-diagnosis, moreover incorrect contact details, lost cellphones, disconnected cellphone numbers, changes in physical address and the likelihood of most patients using prepaid SIM cards resulting in number hoping made tracking of patients difficult. The proportion deceased in this study maybe underestimated as the high number of disconnected cellphone numbers is perhaps indicative of death particularly in the more advanced patients. [8] We were unable to trace 19% of patient folders to validate clinic attendance as these were either misplaced at the clinic or participants provided us with incorrect clinic information. Recall and social desirability bias may have also influenced findings pertaining to disclosure, clinic visit, reasons for failing to link to care. Majority of the drop-out occurred in the ≥351 cells/μl stratum as 32% in individuals in this group did not receive a CD4 count and almost a third (63.6%) failed to link to care. However, due to sampling a small proportion (30%) in the highest CD4 count bracket, both these effects might be diluted. If all individuals in the ≥351 cells/μl stratum were sampled, drop-out at both steps would have been considerably higher.If linkage to care among those who did not receive a CD4 count was examined, and then findings could potentially reveal a lower linkage in this group because they did not receive additional post-test counselling from staff (appendix 13). The number of follow-up attempts and the degree of post-test counselling per stratum may have acted as a potential confounders however this data was not routinely and rigorously collected on this mobile unit.

Strengths of the study included that clinic folder reviews were performed to verify self-reported linkage to HIV care. Trained bilingual counsellors were employed to minimise respondent bias and no incentives were received for participation. The mobile HIV testing services and HIV care at public healthcare facilities that these individuals accessed were free of charge therefore our results could be generalised to a similar setting. Inclusion of those who did not have a CD4 count done may have not influenced the main study outcome (linkage to care) considerably as they possessed a similar demographic and clinical profile to those who had a CD4 count done (appendix 10). The 76 randomly selected HIV+ individuals were similar to the base population from which they were drawn (appendix 12).

In conclusion, findings from this study indicate that linkage to care from a mobile testing unit is feasible. In the cascade from HIV testing to care, one area of attrition is the delivery of CD4 count results which can be remedied with the use of reliable POC CD4 count testing. Linkage to HIV care was shown to be inversely related to CD4 count result. Of note, ART-eligible patients linked to care best but this study also indicates delays in ART commencement among these patients which could adversely affect outcomes. Other areas for intervention include improving healthcare access for

employed HIV-infected individuals, and ensuring health staff emphasise the need to link to care despite feeling well and having a high CD4 count.

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AUTHORS CONTRIBUTION

DG: (research co-ordinator) managed the study team and the data, assisted with follow-ups, conducted clinic folder reviews as well as statistically analysed the data and wrote all drafts of the manuscript. NVS: managed the mobile testing unit, assisted with the interpretation of results and reviewed all drafts of the manuscript. KK: provided guidance to the study design, statistical analysis, and interpretation of results as well as reviewed all drafts of the manuscript. CM: co-supervised the study, assisted with the study design and statistical analysis as well as reviewed all drafts of the manuscript. LGB: supervised the study, contributed to the study design, interpretation of results as well as reviewed all drafts of the manuscript. RW: reviewed the final manuscript. All authors have reviewed the manuscript and given final approval.

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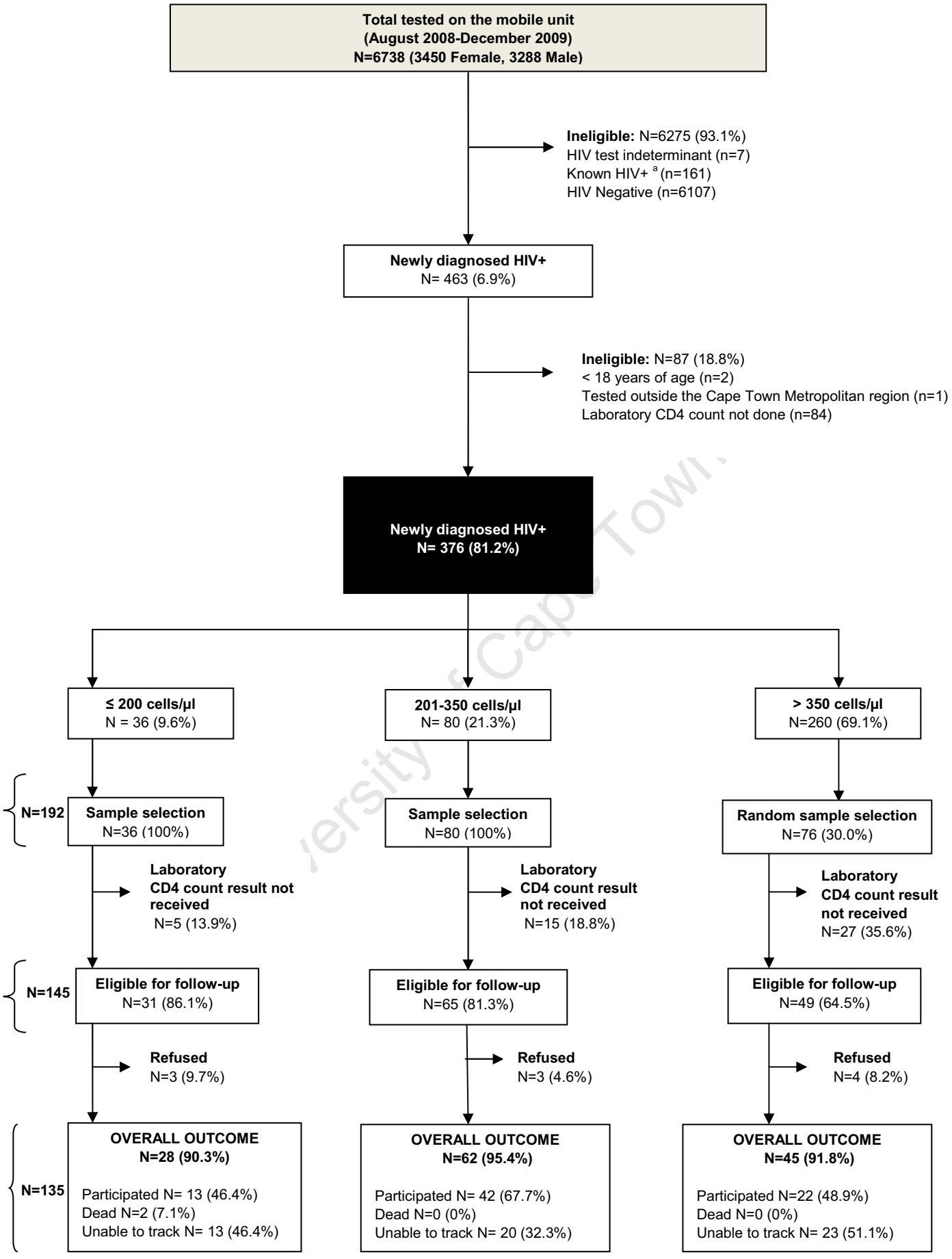

Figure1: **Schematic representation of study's inclusion and exclusion criteria for each stage of the analysis, sampling procedure and overall outcome for each CD4 count strata. a) HIV+= HIV positive**

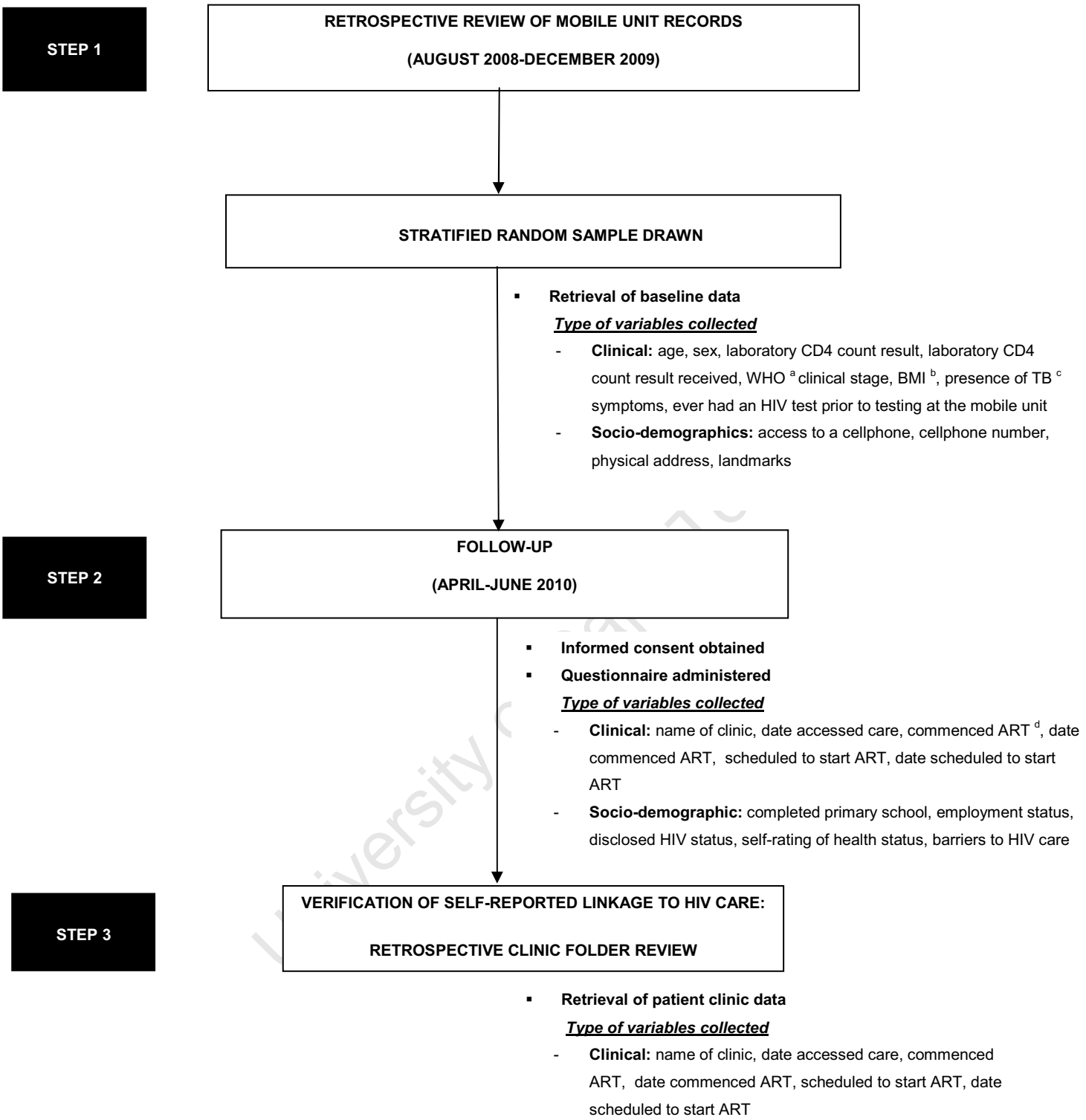

Figure 2: Flow diagram illustrating the study procedures, points of data collection and types of variables collected. a) WHO= World Health Organisation, b) BMI= Body Mass Index, c) TB= Tuberculosis and d) ART= antiretroviral therapy

Table 1: Description of baseline characteristics for those newly-diagnosed with HIV on the mobile unit and had a laboratory CD4 count done (N=192).

Variable	Total N=192 % (95% CI) [a]	CD4 ≤ 200 cells/µl (n=36) % (n)	CD4 201-350 cells/µl (n=80) % (n)	CD4 > 350 cells/µl (n=76) % (n)
Laboratory CD4 count result received	72.8 (65.0-80.5)	86.1 (31)	81.3 (65)	68.1 (49)
Access to a cellphone	81.8 (75.2-88.4)	91.7 (33)	82.5 (66)	80.3 (61)
Female	60.5 (52.3-68.7)	66.7 (24)	57.5 (46)	60.5 (46)
Mean age	34.8 (33.1-36.5)	37.1	36.2	34.1
Ever had an HIV test prior to testing at the mobile unit	60.2 (52.2-68.2)	40.0 (14)	48.1 (38)	66.7 (50)
Mean laboratory CD4 count (cells/µl)	488.6 (457.5-519.6)	134.6	279.1	602.0
WHO [b] clinical stage (I vs. II, III and IV)	60.4 (52.5-68.3)	34.3 (12)	45.6 (36)	68.4 (52)
Mean BMI [c]	26.7 (25.7-27.7)	27.1	27.2	26.5
Presence of TB [d] symptoms	20.7 (14.4-27.1)	41.7 (15)	32.4 (24)	14.1 (10)

a) 95% CI= 95% Confidence Interval, b) WHO= World Health Organisation, c) BMI= Body Mass Index and d) TB= Tuberculosis

Table 2: Binomial regression models to assess the likelihood of receiving a laboratory CD4 count result among individuals newly-diagnosed with HIV on the mobile unit (N=145).

Variable	Univariate analysis RR [a] (95% CI) [b]	Bivariate analysis [c] RR (95% CI)	Multivariate analysis [c, d] RR (95% CI)
Laboratory CD4 count (cells/µl)			
CD4 ≤ 350	1		1
CD4 > 350	0.82 (0.69-0.98) [1]		0.85 (0.73-0.99) [4]
Sex			
Male		1	1
Female		1.19 (1.01-1.40) [2]	1.09 (0.95-1.24)
Age			
≤30 years		1	
≥ 31 years		1.04 (0.88-1.24)	
Has a cellphone			
No		1	1
Yes		2.71 (1.58-4.65) [3]	2.64 (1.54-4.53) [5]

a) RR= Risk Ratio, b) 95% CI= 95% Confidence Interval, c) all variables in the bivariate and multivariate analysis were adjusted for laboratory CD4 count and d) variables assessed in the multivariate analysis: laboratory CD4 count, sex and has a cellphone.

1: P= 0.032, 2: P= 0.041, 3: P= 0.001, 4: P=0.001 and 5: P= 0.032

Table 3: Description of clinical and socio-demographic data for newly-diagnosed HIV+ individuals that received their laboratory CD4 count result and participated (N=77).

Variable	Total N= 77 % (95% CI) [a]	CD4 ≤ 200 cells/µl (n=13) % (n)	CD4 201-350 cells/µl (n=42) % (n)	CD4 > 350 cells/µl (n=22) % (n)
Female	72.0 (59.6-84.3)	76.9 (10)	69.1 (29)	72.7 (16)
Mean age	36.6 (33.7-39.6)	39.1	36.6	36.2
WHO [b] clinical stage (I vs. II, III and IV)	63.5 (50.9-76.1)	53.9 (7)	50.0 (21)	72.7 (16)
Mean laboratory CD4 count (cells/µl)	432.8 (387.2- 478.4)	123.4	288.0	567.1
Mean BMI [c]	28.2 (26.3-30.0)	27.7	27.9	28.5
Presence of TB [d] symptoms	24.4 (13.7-35.1)	53.9 (7)	33.3 (13)	14.3 (3)
Ever had an HIV test prior to testing at the mobile unit	60.3 (47.0-73.7)	58.3 (7)	50.0 (21)	66.7 (14)
Completed primary school	84.8 (74.4-95.2)	83.3 (10)	90.5 (38)	81.8 (18)
Unemployed	50.1 (36.3-63.8)	76.9 (10)	50.0 (21)	45.5 (10)
Informal dwelling	64.4 (51.2-77.7)	53.9 (7)	69.1 (29)	63.6 (14)
Disclosed one's HIV status	69.3 (56.5-82.1)	69.2 (9)	71.4 (30)	68.2 (15)
Self-rating of health status (strong vs. average and weak)	73.8 (62.0-85.6)	69.2 (9)	69.1 (29)	77.3 (17)
Linked to HIV care	52.5 (39.4-65.6) [e]	100.0 (13)	66.7 (28)	36.4 (8)
Mean time (months) from diagnosis to accessing HIV care	2.2 (0.3- 4.0)	0.6	2.0	3.0
On ART [e]		69.2 (9)	N/A	N/A
Mean time (months) from accessing care to starting ART	1.9 (0.6-3.1)	1.9	N/A	N/A
Mean time (months) from diagnosis to starting ART	4.3 (2.1-6.5)	4.3	N/A	N/A
Scheduled to start ART		30.8 (4)	N/A	N/A
Failed to link to HIV care	47.5 (34.4-60.6)	0	33.3 (14)	63.6 (14)
Barriers to HIV care:				
Work during the day and cannot get time off to visit the clinic	41.4 (21.9-61.0)	N/A	25.0 (5)	47.1 (8)
Clinic too far away from work	15.7 (0.9-30.5)	N/A	10.0 (2)	17.7 (3)
Fear toxicity and side effects of ART	12.6 (0.3-25.5)	N/A	15.0 (3)	11.8 (2)
Fear of disclosure of one's HIV status/stigma associated with being HIV+ [f] /social isolation	8.8 (3.4-20.9)	N/A	0	11.8 (2)

a) 95% CI= 95% Confidence Interval, b) WHO= World Health Organisation, c) BMI= Body Mass Index, d) TB= Tuberculosis, e) ART= Antiretroviral Therapy and f) HIV+= HIV Positive

Table 4: Binomial regression models to assess the likelihood of linking to care among newly-diagnosed HIV+ individuals that received a laboratory CD4 count (N=77).

Variable	Univariate analysis RR [a] (95% CI) [b]	Bivariate analysis [c] RR (95% CI)
Laboratory CD4 count (cells/ µl)		
CD4 ≤ 350	1	
CD4 > 350	0.49 (0.27-0.87) [1]	
Sex		
Male		1
Female		1.18 (0.81-1.72)
Age		
≤30 years		1
≥ 31 years		1.21 (0.83-1.77)
WHO [d] clinical stage		
II, III and IV		1
I		0.88 (0.65-1.18)
Presence of TB [e] symptoms		
No		1
Yes		1.45 (1.11-1.90) [2]
Disclosed one's HIV status		
No		1
Yes		1.57 (0.99-2.48) [3]
Self-rating of health status		
Weak and average		1
Strong		1.00 (0.72-1.38)
Dwelling		
Informal		1
Formal		1.05 (0.78-1.42)
Completed primary school		
No		1
Yes		1.17 (0.66-2.08)
Employment Status		
Unemployed		1
Employed		0.72 (0.51-1.01) [4]

a) RR= Risk Ratio, b) 95% CI= 95% Confidence Interval, c) all variables in the bivariate analysis were adjusted for laboratory CD4 count, d) WHO= World Health Organisation and e) TB= Tuberculosis

1: P= 0.014, 2: P= 0.007, 3: P= 0.054 and 4: P= 0.056

PART D: APPENDICES

PART D: APPENDICES

APPENDIX 1: INFORMATION SHEET AND INFORMED CONSENT

DESMOND TUTU HIV FOUNDATION
STUDY- LINKAGE TO CARE: FROM HIV TESTING AND COUNSELLING TO CARE
INFORMATION SHEET

1) Why are we doing this study?

HIV/AIDS is a serious problem in our country and more needs to be done to improve the lives of those living with HIV/AIDS. The Desmond Tutu HIV Foundation (DTHF) is trying to find the best way to help those with HIV/AIDS enter an HIV program at a clinic.

We would like to follow-up on our Tutu Tester clients that tested positive for the first time and received their lab CD4 count result. Firstly, we would like to determine how many attended a clinic and if not, the reasons that prevented them from doing so. Secondly, we would like to know how many of these clients started antiretrovirals (ARVs).

2) What will taking part in the study involve?

Once you have provided us with informed consent you will be asked to answer a few questions about your clinic visit.

If you have not gone to a clinic we would like to know what stopped you from attending. Even if you have attended but failed to continue going, we would like to know the reasons for not remaining in care. We would also like to know if you are using your Road to HIV Health Card and the quality of service you received by the Tutu Tester.

If you give us permission, we will contact your clinic to confirm information on your clinic visit (i.e. name of clinic, date of first visit to the clinic, clinic folder number, is client still attending the clinic, has the client had more than one visit to the clinic in the last six months, was blood taken for a CD4 count, time to next CD4, where ARVs commenced, time to ART, is client still taking ARVs).

It is important that you know the following:

- You can still participate in this study even if you decide not to give us permission to contact your clinic. This will in no way affect the care you receive at the clinic or Tutu Tester as well as your rights as a participant.
- There are no physical interventions in this study including no bloods or medication.
- You will not be given any form of reimbursement such as money or gifts if you decide to participate in this study.
- If you do not take part, no-one will find out that you did so and it will not change the care that you receive at the clinic or at the Tutu Tester.

3) What are the risks of taking part in this study?

Some people may be curious to know why we are contacting you and this may be difficult to answer. However, we can help you decide on how you will give information about this study to your partner, family or friends.

4) What are the benefits of taking part in this study?

You and others living with HIV could benefit in the future from facts learned in this study. These facts may help come up with new ways to encourage people living with HIV to attend clinics immediately and have their health monitored regularly.

5) Is your information confidential?

All information collected about you will be kept confidential. The information will be stored at the DTHF in a locked cupboard and will only be accessible to the study staff. All data forms (except the informed consent form) will not contain your name and address because you will be identified only by your special study number, which will be known only to you and the study staff.

6) Whom can you contact about the study?

If you have a problem related to being in the study, please call Darshini Govindasamy or Prof Linda-Gail Bekker (Principal Investigator) at (021) 633 6599. You can also contact the Tutu Tester on 071 685 3417 if you would like to talk to one of the counsellors about anything else.

If you have any questions about your rights as a research subject, please call Dr Blockman, the Chair of the Ethics Committee at (021) 406 6492.

INFORMED CONSENT FORM

A. HOME VISIT

Participant:

I, **(Name and Surname of participant)**

_____agree to participate in this research study.

I specifically consent to the study team to contact my clinic in order to verify information about my visits: **(mark with an X)**

YES ☐ **NO** ☐

I understand that my participation is voluntary and that I may withdraw from the research study at any time and for any reason and this will not affect the legal rights I may otherwise have.

Print Name: _____ **Signature:** _____

Date: |____|____| /|____|____|____|/|____|____|____|____|

B. TELEPHONICALLY

Study staff obtaining verbal consent:

(Name and Surname of participant)_____has agreed to participate in this research study.

Client has consented to the study team to contact his/her clinic in order to verify information about clinic visits: **(mark with an X)**

YES ☐ **NO** ☐

I have explained the nature, demands and foreseeable risks of this study to the above volunteer.

Print Name: _____ **Signature:** _____

Date: |____|____| /|____|____|____|/|____|____|____|____|

APPENDIX 2: CLIENT FORM REVIEW:

(Please indicate with tick where applicable)

1) IDENTITY:	
a) Tutu Tester Client number	|___|___|___|___| |___|___|___|___|
b) Date of initial Tutu Tester visit	|___|___| /|___|___|___|/|___|___|___|___|
a) Study number	|___|___|___|

2) DEMOGRAPHICS:				
a) Date of birth	|___|___| /|___|___|___|/|___|___|___|___|			
b) Sex	**M**		**F**	

3) WHO CLINICAL STAGE & LAB CD4 COUNT RESULT:							
a) WHO clinical stage	**1**		**2**		**3**		**4**	
b) Lab CD4 count result (cells/µl)								
c) Lab result given to client	**Y**		**N**					
If Yes, Date result given to patient	|___|___| /|___|___|___|/|___|___|___|___|							

4) METHOD OF CONTACT	
a) In person	
b) Telephonic	
c) Clinic staff phoned for result	
▪ Name of Clinic	
▪ Nurse/Doctor's name	
▪ Date given	|___|___| /|___|___|___|/|___|___|___|___|
e) Clinic most likely to use	
	Folder #:
f) Hospital most likely to use	
	Folder #:
g) Additional Information	

5) REFERRED FOR:						
a) Routine HIV care and follow-up						
b) Enrolment in ARV programme						
c) Urgent ARV work up						
d) Other	TB screening		STI		Pregnancy	
	Pap smear		Hypertension		Diabetes Mellitus	
	Family Planning		Obesity		Anaemia	
	Nutrition counselling					
e) Tested For TB	Y		N			
f) Overall TB Result	Smear Pos		Culture Pos		Negative	
g) Road to HIV Health Card given	Y		N		UNK	
h) Other						

APPENDIX 3: QUESTIONNAIRE

(Please indicate with a tick where applicable)

1) IDENTITY:	
b) Tutu Tester Client Number	|___|___|___|___| |___|___|___|___|
c) Date of initial Tutu Tester visit	|___|___| /|___|___|___|/|___|___|___|___|
d) Study number	|___|___|___|

2) INTERVIEW DETAILS				
a) Date of interview	|___|___| /|___|___|___|/|___|___|___|___|			
b) Name of interviewer				
c) Interview Method	Telephonic		Face-to-face	

3) DEMOGRAPHICS:				
a) Date of birth	|___|___| /|___|___|___|/|___|___|___|___|			
b) Sex	**M**		**F**	
c) Are you South African	**Y**		**N**	

4) SOCIOECONOMICS:				
a) Are you employed	**Y**		**N**	
	Monthly income	**R**		
b) Did you complete primary school	**Y**		**N**	
c) Where do you live				
d) Do you live in a formal dwelling or informal dwelling?	**F**		**I**	

5) HIV STATUS:						
a) Have you disclosed your status	**Y**			**N**		
b) Do you feel stigmatised after having disclosed	**Y**			**N**		
c) Would you rate your current health as strong/average/weak	**S**		**A**		**W**	

6) LINKAGE TO CARE AND TREATMENT:				
6.1) Did you attend clinic/hospital after	**Y**		**N**	

having been tested on the Tutu Tester				
6.2) If Yes:				
6.2.1) Lab CD4 > 200 cells/µl				
a) Name of Clinic				
b) Date of first visit to the clinic	|___|___| /|___|___|___|/|___|___|___|___|			
c) Clinic Folder number				
d) Are you still attending the clinic	**Y**		**N**	
e) > One visit in the last six months	**Y**		**N**	
	How many			
f) Was blood taken for a CD4 count	**Y**		**N**	
	Last CD4 count result (cells/µl)			
g) Time to next CD4	|___|___| /|___|___|___|/|___|___|___|___|			
6.2.2) Lab CD4 count <200 cells/µl Or Stage 4				
a) Name of Clinic				
b) Date of first visit to the clinic	|___|___| /|___|___|___|/|___|___|___|___|			
c) Clinic Folder number				
d) Are you still attending the clinic	**Y**		**N**	
e) > One visit in the last six months	**Y**		**N**	
	How many			
f) Was blood taken for a CD4 count	**Y**		**N**	
	Last CD4 count result (cells/µl)			
g) Time to next CD4	|___|___| /|___|___|___|/|___|___|___|___|			
h) Where ARVs commenced	**Y**		**N**	
	Date	|___|___|/|___|___|___|/|___|___|___|___|		
i) Time to ART	|___|___|/|___|___|___|/|___|___|___|___|			
j) Still taking ARVs	**Y**		**N**	
	Can identify medication	**Y**		
		N		

6.3) If No, what were the obstacles to care	
a) Live too far away from clinic	
b) Too sick to travel	
c) Cannot afford transport costs	
d) Work during the day and cannot get time off to visit the clinic	
e) Clinic too far away from work	
f) Have no one to take care of dependants (baby/kids/elderly/sick/disabled family member)	
g) Fear disclosure/stigma/social isolation	
h) Fear discrimination because not South African	
i) Do not see the need to attend	
j) Do not feel ready to start life long treatment	
k) Fear toxicity and side-effects of ARVs	
l) Want to complete TB treatment before starting ARVs	
m) Other	

7) ROAD TO HIV HEALTH CARD:				
a) Did you present it to the clinic	**Y**		**N**	
b) Are you still using it	**Y**		**N**	
c) Is it helpful and easy to use	**Y**		**N**	

8) TUTU TESTER SERVICE:						
a) How would you rate the service you received from staff (Good/ Average/ Poor)	**G**		**A**		**P**	
b) Did the referral process help	**Y**				**N**	
	How					

APPENDIX 4: CLINIC ATTENDANCE FORM

(Please indicate with a tick where applicable)

1) IDENTITY:	
a) Tutu Tester Client number	|___|___|___|___| |___|___|___|___|
b) Study number	|___|___|___|

2) CLINIC DETAILS:					
a) Name of Clinic					
b) Contact Number					
c) Interview Method	**Telephonic**		**Face-to-face**		
d) Name of Interviewee					
e) Name of Interviewer					
f) Date of interview	|___|___| /|___|___|___|/|___|___|___|___|				

3) LINKAGE TO CARE AND TREATMENT:							
3.1) Did the client attend the clinic	**Y**		**N**				
3.2) If Yes:							
3.2.1) Lab CD4 > 200 cells/µl							
a) Date of first visit to the clinic	|___|___| /|___|___|___|/|___|___|___|___|						
b) Clinic Folder number							
c) Is client still attending the clinic	**Y**		**N**				
d) > One visit in the last six months	**Y**		**N**				
	How many						
e) Was blood taken for a CD4 count	**Y**		**N**				
	Last CD4 count result (cells/µl)						
f) Time to next CD4	|___|___| /|___|___|___|/|___|___|___|___|						
3.2.2) Lab CD4 count <200 cells/µl Or Stage 4							
a) Date of first visit to the clinic	|___|___| /|___|___|___|/|___|___|___|___|						
b) Clinic Folder number							
c) Is client still attending the clinic	**Y**		**N**				
d) > One visit in the last six months	**Y**		**N**				
	How many						
e) Was blood taken for a CD4 count	**Y**		**N**				
	Last CD4 count result (cells/µl)						
f) Time to next CD4	|___|___| /|___|___|___|/|___|___|___|___|						
g) Where ARVs commenced	**Y**		**N**				
	Date	|___|___|/|___|___|___|/|___|___|___|___|					
h) Time to ART	|___|___| /|___|___|___|/|___|___|___|___|						
i) Still taking ARVs	**Y**		**N**				

UNIVERSITY OF CAPE TOWN

Health Sciences Faculty
Research Ethics Committee
Room E52-24 Groote Schaur Hospital Old Main Building
Observatory 7925
Telephone [021] 406 6626 • **Facsimile** [021] 406 6411
e-mail: shuneta.thomas@uct.ac.za

29 March 2010

REC REF: 007/2010

Prof LG Bekker
Desmond Tutu, HIV Centre
IIDMM
Medical School

Dear Prof Bekker

PROJECT TITLE: LINKAGE TO CARE: FROM HIV TESTING AND COUNSELLING TO CARE.

Thank you for your e-mail to the Research Ethics Committee dated 25th March 2010.

It is a pleasure to inform you that the Ethics Committee has **noted and approved** the following for the above-mentioned study:

1. Protocol study – Linkage to Care: From HIV Testing and counselling to care version 2, March 2010
2. Information Sheet and Informed Consent Form, Study – Linkage to care: From HIV Testing and counselling to care version 3.0, March 2010

In future, please use our amendment forms as these allow you to complete all the above detailed information which, in turn, results in unnecessary duplication.

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please quote the REC. REF in all your correspondence.

Yours sincerely

Oakley Blockman

pp **PROFESSOR M BLOCKMAN**
CHAIRPERSON, HSF HUMAN ETHICS

S Thomas

Appendix 5: Research ethics approval letter: University of Cape Town, Human Research Ethics Committee

Verwysing
Reference 19/18/RP49/2010
Isalathiso

Navrae
Enquiries Dr A Dearham
Imibuzo

Telefoon
Telephone 021 483 4198
Ifowuni

Departement van Gesondheid
Department of Health
iSebe lezeMpilo

PO BOX 13801
MOWBRAY 7705
CAPE TOWN
SOUTH AFRICA

FAX: **(021) 633-0182**

Dear **Prof Linda-Gail Bekker**
Prof Catherine Mathews
Darshini Govindasamy

RE: ***Linkage To Care: From HIV Testing and Counselling To Care***

Thank you for submitting your proposal to undertake the above-mentioned study. We are pleased to inform you that the department has granted you approval for your research. Please contact the following people to assist you with access to:

Delft CHC	**Mr Jaco van Heerden**	**Tel: (021) 954 2237**
Crossoads CHC	**Mr David Binza**	**Tel: (021) 386 1119 / 385 0260**

Kindly ensure that the following are adhered to:

1. Arrangements can be made with managers, providing that normal activities at requested facilities are not interrupted.
2. Researchers, in accessing provincial health facilities, are expressing consent to provide the department with an electronic copy of the final report within six months of completion of research. This can be submitted to the provincial Research Co-ordinator (healthres@pgwc.gov.za).
3. The reference number above should be quoted in all future correspondence.

We look forward to hearing from you.

Yours sincerely

DR J CUPIDO
DEPUTY-DIRECTOR GENERAL
DISTRICT HEALTH SERVICES AND PROGRAMMES
DATE: 22.06.2010

CC: DR J. CLAASSEN **DIRECTOR: KLIPFONTEIN/MITCHELL'S PLAIN SUB-STRUCTURES**
DR L. BITALO **DIRECTOR: NORTHERN/ TYGERBERG SUB-STRUCTURES**

Dorpstraat 4
Posbus 2060
KAAPSTAD
8000

4 Dorp Street
PO Box 2060
CAPE TOWN
8000

Appendix 6: Research ethics approval letter: The Western Cape Department of Health- Provincial Research Ethics Committee

CITY OF CAPE TOWN | ISIXEKO SASEKAPA | STAD KAAPSTAD

Civic Centre
12 Hertzog Boulevard
Cape Town 8001
P O Box 298, Cape Town 8000
Ask for: Dr H Visser
Tel: 021 400-3981
Cell: 083 298 8718
Fax: 021 421-4894

Ibhloko leLunta
12 Hertzog Boulevard
iKapa 8001
P O Box 298, Cape Town 8000
Cela: Grh H Visser
Umnxeba: 021 400-3981
Cell: 083 298 8718
Ifeksi: 021 421-4894

Burgersentrum
Hertzog-boulevard 12
Kaapstad 8001
Posbus 298, Kaapstad 8000
Vra vir: Dr H Visser
Tel: 021 400-3981
Sel: 083 298 8718
Faks: 021 421-4894

E-mail: helene.visser@capetown.gov.za
Website: www.capetown.gov.za
Ref:
Filename: \\chb-civic-539\Home$\kgeorge\My Documents\EGeorge\Research Projects\Lgbekker.docx

CITY HEALTH — City Health

2010-04-07

re: Research Proposal: Linkage to Care: From HIV testing and counselling to care (ID No: 10174)

Dear Prof Bekker,

Permission has been granted for you to do the research as set out in your protocol at the following City Health Clinics:

Southern Sub District:	**Hout Bay Main Rd, Masiphumelele & Lotus River Clinics**
Contact People:	Mrs L Bakana (Sub District Manager) Tel: (021) 710-8295 / 083 333 4942 Mrs B van Niekerk (Head: PHC & Programmes) Tel: (021) 710-9383 / 082 821 7361
Klipfontein Sub District:	**Vuyani, Nyanga & Masincidane Clinics**
Contact People:	Mr K Nkoko (Sub District Manager) Tel: (021) 630-1667 / 082 433 1332 Ms T Jantjies (Head: PHC & Programmes) Tel: (021) 630-1626 / 084 220 0133

Please note the following:

1. All individual patient information obtained must be kept confidential.
2. Access to clinics and its patients must be arranged with the relevant Managers such that normal activities are not disrupted.
3. A copy of the final report must be sent to City Health Head Office (P. O. Box 2815, Cape Town 8001) within 3 months of its completion and feedback must also be given to the clinics involved.
4. Your project has been given an ID number (10174). Please use this in any future correspondence with us.

Thank you for your co-operation and please contact me if you require any further information or assistance.

Yours sincerely

DR G H VISSER
MANAGER: SPECIALISED HEALTH

cc. Mrs Bakana & Mrs van Niekerk
Mr Nkoko & Ms Jantjies
Dr Jennings
Ms Caldwell
Prof C Mathews
Ms D Govindasamy

Appendix 7a: Research ethics approval letter: The City Health Department of Cape Town- Research Ethics Committee

CITY OF CAPE TOWN | ISIXEKO SASEKAPA | STAD KAAPSTAD

Civic Centre
12 Hertzog Boulevard
Cape Town 8001
P O Box 2815, Cape Town 8000
Ask for: Dr G H Visser
Tel: 021 400-3981
Cell: 083 298 8718
Fax: 021 421-4894
E-mail: helene.visser@capetown.gov.za
Website: http://www.capetown.gov.za
Ref:
Filename: F:\Research\DGovindasamy10174.docx

Iziko loLuntu
12 Hertzog Boulevard
Cape Town 8001
P O Box 2815, Cape Town 8000
Cela: Qrh G H Visser
Umxeeba: 021 400-3981
Cell: 083 298 8718
Ifeksi: 021 421-4894

Burgersentrum
Hertzog-boulevard 12
Kaapstad 8001
Posbus 2815, Kaapstad 8000
Vra vir: Dr G H Visser
Tel: 021 400-3981
Sel: 083 298 8718
Faks: 021 421-4894

CITY HEALTH — Specialised Health

2010-07-02

re: Permission to access Clinic Folder Reviews for Study 10174 (Linkage to care: From HIV Testing and Counselling to Care) at 11 additional sites

Dear Darshini,

Permission has been granted for you to access 11 additional City Health Clinics.

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Thank you for your co-operation and please contact me if you require further assistance or information.

Appendix 7b: Research ethics approval letter: The City Health Department of Cape Town- Research Ethics Committee

AUTHOR		**YEAR**		**COUNTRY**	
SETTING		**STUDY POPULATION**		**STUDY DESCRIPTION**	
OUTCOME MEASURE	1)				
OUTCOME MEASURE:	2)				
GROUP:	**1) Test-Register , 2) Test-CD4 testing, 3) Screen-Pre-ART care 4) Screen-ART care**				
Quantitative	**Y N**	**Source of outcome measure**			
Qualitative	**Y N**	**Source of outcome measure**			
Year of cohort		**Period of recruitment**		**Period of follow-up**	
Sample size eligible		**Sample size participated**			

STEPS	**LOSSES**	**TIME TO CARE**

STEP	**RISK FACTORS**

	PSYCHO-SOCIAL	**HEALTH SYSTEM**	**ORGANISATIONAL**
Barriers:	1.	1.	1.
	2.	2.	2.
	3.	3.	3.
Facilitators:	1.	1.	1.
	2.	2.	2.

Quality assessment	***TOTAL=***		
Research question	***POINT=***		
The study addresses an appropriate and clearly focused question+	0	0.5	1
The study is relevant to the needs of the project+	0	0.5	1
Selection of the Subjects	***POINT=***		
The individuals selected are comparable in all respects with the source population (the population the results will be generalised to)+	0	0.5	1
The study indicates how many of the individuals asked to take part did so/analysed*	0	0.5	1
The study indicates what percentage of individuals recruited dropped out before the study was completed & reasons for non-participation/recruited*	0	0.5	1
The study indicates the percentage of participants followed-up and outcome*	0	0.5	1
Comparison is made between full participants and those lost to follow up*	0	0.5	1
Assessment	***POINT=***		
The outcomes are clearly defined+	0	0.5	1
The measure of assessment is reliable+	0	0.5	1
Evidence from other sources is used to demonstrate that the method of outcome assessment is valid and reliable*	0	0.5	1
Followed-up those who did not initiate ART/link to care *	0	0.5	1
Described method of follow-up+	0	0.5	1
Gives characteristics of study participants+	0	0.5	1
Indicates missing data for each variable of interest*	0	0.5	1
Limitations discussed+	0	0.5	1
Generalisability discussed+	0	0.5	1
Confounding	***POINT=***		
The main potential confounders are identified and taken into account in the design and analysis*	0	0.5	1
Statistical Analysis	***POINT=***		
Confidence intervals are provided*	0	0.5	1
P values are provided*	0	0.5	1

+: Criterion assessed in both quantitative and qualitative studies
*: Criterion assessed only in quantitative studies

Appendix 8: Data extraction sheet and quality assessment tool used to assess the methodological quality of each study

Appendix 9: Instruction for authors for Journal of Acquired Immune Deficiency Syndromes

SCOPE

JAIDS: Journal of Acquired Immune Deficiency Syndromes is a peer-reviewed, multidisciplinary journal directed to an audience of physicians and researchers. The journal publishes original work in the form of Original Articles, Implementation and Operational Research*, Rapid Communications, Critical Reviews, Brief Reports, and Letters to the Editor*. *JAIDS* does not publish case reports. (*published online only)

MANUSCRIPT SUBMISSION

A submitted manuscript must be an original contribution not previously published (except as an abstract or preliminary report), must not be under consideration for publication elsewhere, and, if accepted, must not be published elsewhere in similar form, in any language, without the consent of Lippincott Williams & Wilkins. Each person listed as an author is expected to have participated in the study to a significant extent. Although the editors and referees make every effort to ensure the validity of published manuscripts, the final responsibility rests with the authors, not with the journal, its editors, or the publisher.

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An author is considered to be someone who has made substantive contributions to a published study. Each author should have participated sufficiently in the work to take public responsibility for appropriate portions of the content. More specifically, authorship credit requires *a*) substantial contributions to conception and design, or acquisition of data, or analysis and interpretation of data; *b*) drafting the paper or revising it critically for important intellectual content; and *c*) final approval of the version to be published. Contributors must meet conditions for *a, b*, and *c*—all 3—to be eligible for authorship. All persons listed as authors must meet the 3 criteria above, and all persons who meet the above criteria must be listed as authors. Please note that acquisition of funding, collection of data, or general supervision of a research group, alone, does not justify authorship. For large, multicenter group studies, individuals who accept direct responsibility for the manuscript must be identified. Those individuals will be required to complete the ***JAIDS*** Copyright Transfer Agreement. Contributors who do not meet the criteria for authorship should be listed in the acknowledgments section. Persons providing technical help, writing assistance, or a department chair providing general support are examples of persons who should not be included as authors, but who should be listed in the Acknowledgments section.

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Original Articles	3500 words + 5 figures/tables - if more then use Supplemental Digital Content	Structured; 250 words
Implementation and Operational Research *(published online only)*	3500 words + 5 figures/tables - if more then use Supplemental Digital Content	Structured; 250 words
Rapid Communications	2000 words + 2 figures/tables	Unstructured, 150 words
Critical Reviews	3000 words + 2 figures/tables	Unstructured; 150 words
Brief Reports	2000 words + 2 figures/tables	Unstructured; 100 words
Letter to the Editor *(published online only)*	1500 words; 1 figure/table	none

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The above guidelines apply to the original article format. Articles should be limited to 3500 words + 5 figures/tables. If additional space is needed, then use Supplemental Digital Content options. There should be a structured abstract of 250 words or less.

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All manuscripts should be submitted through one of the existing three sections: Basic and Translational Science, Clinical Science, or Epidemiology and Prevention using the article type Implementation and Operational Research. Structure of article is the same as Original Article.
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Journal Article

1. Schambelan M, Benson CA, Carr A, et al. Management of metabolic complications associated with antiretroviral therapy for HIV-1 infection: recommendations of an International AIDS Society-USA panel. *J Acquir Immune Defic Syndr.* 2002;31:257–275.

Book Chapter

2. Wortmann RL, Bentzel CJ. Renal handling of uric acid. In: Massry SG, Glassock RJ, eds. *Massry and Glassock's Textbook of Nephrology*. Phiadelphia: Lippincott Williams & Wilkins, 2001;90–92.

Entire Book

3. Mandell GL, Mildvan D, eds. *Atlas of AIDS*. 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 2001.

Software

4. Epi Info [computer program]. Version 6. Atlanta: Centers for Disease Control and Prevention, 1994.

Online Journals

5. Friedman SA. Preeclampsia: a review of the role of prostaglandins. *Obstet Gynecol* [serial online]. January 1988;71:22–37. Available from: BRS Information Technologies, McLean, VA. Accessed December 15, 1990.

Database

6. CANCERNET-PDQ [database online]. Bethesda, MD: National Cancer Institute, 1996. Updated March 29, 1996.

World Wide Web

7. Panel on Clinical Practices for the Treatment of HIV Infection. Guidelines for the use of antiretroviral agents in HIV-infected adults and adolescents. Department of Health and Human Services and Henry J. Kaiser Foundation, January 28, 2000. Available at: http://www.hivatis.org/guidelines/AA599.pdf.

Paper Presented at a Conference

8. Koenig L, Ellerbrock T, Pratt-Palmire M, et al. Prospective predictors of medication adherence: a study of the first six months of highly active antiretroviral therapy (HAART) using electronic monitoring [WePeB5818]. Presented at: XIV International AIDS Conference; 2002; Barcelona.

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Pattern manuscript style after the *American Medical Association Manual of Style* (9th edition). Stedman's Medical Dictionary (28th edition) and Merriam-Webster's Collegiate Dictionary (11th edition) should be used as standard references. Refer to drugs and therapeutic agents by their accepted generic or chemical names, and do not abbreviate them. Use code numbers only when a generic name is not yet available. In that case, supply the chemical name and a figure giving the chemical structure of the drug. Capitalize the trade names of drugs and place them in parentheses after the generic names. To comply with trademark law, include the name and location (city and state in USA; city and country outside USA) of the manufacturer of any drug, supply, or equipment mentioned in the manuscript. Use the metric system to express units of measure and degrees Celsius to express temperatures, and use SI units rather than conventional units.

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Appendix: 10

Table 1: Distribution of demographic and clinical data amongst newly-diagnosed HIV+ individuals (n=460) stratified by those that had a laboratory CD4 count done (n=376) and those that did not (n=84).

	Total N=460 N (%)	Had a CD4 count done (study group) n=376 (81.8%) n (%)	Did not have a CD4 count done n=84 (18.3%) n (%)
Gender			
Female	271 (58.9)	221 (58.8)	50 (59.5)
Male	189 (41.09)	155 (41.2)	34 (40.5)
Median age (years)	32 (IQR: 26-40)	32 (IQR: 26-39.5)	32 (IQR: 26.5-42.5)
Ever had an HIV test prior to testing at the mobile unit			
Yes	264 (57.4)	162 (43.1)	34 (40.5)
No	196 (42.6)	214 (56.9)	50 (59.2)
WHO clinical stage			
I	259 (56.3)	208 (55.3)	51 (60.7)
II	118 (25.7)	104 (27.7)	14 (16.7)
III	58 (12.6)	53 (14.1)	5 (5.9)
IV	4 (0.9)	3 (0.8)	1 (1.2)
Not done	21 (4.5)	8 (2.1)	13 (15.5)
Mean BMI (kg/m^2)	25.1 (IQR: 22-30.4)	25.1 (IQR:22-30.4)	25.1 (21.9-29.4)
Presence of TB symptoms			
Yes	109 (23.7)	94 (25)	15 (17.9)
No	351 (76.3)	282 (75)	69 (82.1)

Appendix 11: Explanation for the difference in sample size in the protocol and article

The samples size was calculated in early November 2009. It was based on data extracted from the mobile service database. Thus we estimated the number of potentially eligible patients (i.e. newly-identified HIV+ patients that successfully received a CD4 count result) was based on the number seen in previous months.

The sample size in the protocol for newly-identified HIV+ patients that successfully received a CD4 count result (n=225) was relatively higher than the final sample size (n=145) indicated in the manuscript due to several reasons:

1. The mobile service only operated for half the working month in December as the project closed down for the holidays thus the number of potentially eligible clients was considerably lower than previous months.
2. After I obtained research ethics permission to conduct the study I physically retrieved all patient data and cleaned the database. Some patient data was erroneously entered and most patients that received notification of their CD4 count result via post was dropped from the sample as it was not certain whether they received their result or not.

Appendix 12:

Table 2: Description of demographic and clinical data amongst newly-diagnosed HIV+ individuals in the >351 cells/ul stratum (N=263) who were randomly selected (n=76) compared to those that were not selected (n=187).

CD4+ COUNT >=351 cells/ul	TOTAL N=263 N (%)	RANDOMLY SELECTED n=76 (30%) n (%)	UNSELECTED n=187 (70%) n (%)
Median Age (years)	30 (IQR: 26-39)	31 (IQR: 26-38.5)	30 (IQR: 26-39)
Gender			
Male	110 (58.2)	32 (42.1)	78 (41.7)
Female	153 (41.8)	44 (57.9)	109 (58.3)
Median laboratory CD4 count (cells/ul)	563 (IQR: 428-759)	553.5 (IQR: 432.5-759.5)	563 (IQR: 428-759)
Ever had an HIV test prior to testing at the mobile unit			
Yes	165 (62.7)	50 (65.8)	115 (61.5)
No	98 (37.3)	26 (34.2)	72 (38.5)
WHO clinical stage			
I	161 (61.2)	51 (67.1)	110 (58.8)
II	65 (24.7)	19 (25.0)	46 (24.6)
III	30 (11.4)	5 (6.6)	25 (13.4)
IV	7 (2.7)	1 (1.3)	6 (3.2)
Mean BMI	25.1 (IQR: 22.2-30.4)	24.5 (IQR: 21.9-30.8)	25.4 (IQR: 22.3-30.4)
Presence of TB symptoms			
Yes	56 (21.3)	10 (13.1)	46 (24.6)
No	207 (78.7)	66 (86.8)	141 (5.4)

Appendix 13:

Table 3: Distribution of demographic and clinical data amongst newly-diagnosed HIV+ individuals that had a laboratory CD4 count done (n=192), stratified by those who received their CD4 count result (n=145) and those that did not (n=47).

	Total (n=192) % (95% CI)	Laboratory CD4 count result given (n=145) % (95% CI)	Laboratory CD4 count result not given (n=47) % (95% CI)
Access to a cellphone			
Yes	81.8 (75.2-88.4)	94.8 (90.7-98.8)	51.5 (34.8-68.3)
No	18.1 (11.59-24.75)	5.2 (1.1-9.3)	48.5 (31.7-65.2)
Gender			
Female	60.5 (52.3-68.7)	63.7 (54.3-73.1)	52.8 (36.2-69.4)
Male	39.5 (31.3-47.7)	36.3 (26.8-45.7)	47.2 (30.6-63.8)
Mean age	34.8 (33.1-36.5)	35.2 (33.2-37.2)	33.9 (30.5-37.3)
Ever had an HIV test prior to testing at the mobile unit			
Yes	60.2 (52.2-68.2)	61.4 (51.9-70.4)	58 (41.8-74.1)
No	39.8 (31.8-47.8)	38.9 (29.6-48.1)	42.0 (25.8-58.2)
Mean laboratory CD4 count (cells/µl)	488.6 (457.5-519.6)	456.4 (422.2-490.6)	563.9 (496.7-631.2)
WHO clinical stage			
I	60.4 (52.5-68.3)	62.2 (53.2-71.2)	56.2 (40.1-72.2)
II	28.9 (21.5-36.5)	26.7 (18.2-35.0)	34.5 (18.7-50.3)
III	9.8 (5.6-14.0)	10.4 (5.2-15.6)	8.3 (1.1-15.6)
IV	0.8 (0.1-0.20)	0.7 (0.2-1.8)	0.9 (0.9-2.7)
Mean BMI	26.7 (25.7-27.7)	27.2 (26-28.5)	25.4 (23.5-27.2)
Presence of TB symptoms			
Yes	20.7 (14.4-27.1)	20.0 (12.8-27.3)	22.4 (9.5-35.4)
No	79.3 (72.9-85.6)	78 (72.7-87.2)	77.5 (64.5-90.5)

Appendix 14:

Table 4: Definitions of all study outcomes and predictors

OUTCOME	DEFINITION
Laboratory CD4 count result received (Yes)	A newly-diagnosed HIV+ individual who tested at the mobile unit and was subsequently successfully contacted (telephonically or by home visit) and received his/her laboratory CD4 count test result, as documented on the Tutu Tester follow-up form
Laboratory CD4 count result received (No)	A newly-diagnosed HIV+ individual who tested at the mobile unit and could not be traced (telephonically or by home visit) and thus did not receive his/her baseline laboratory CD4 count test result from the Tutu Tester, as documented on the Tutu Tester follow-up form.
Linked to care (Yes)	A newly-diagnosed HIV+ individual who accessed HIV care at a public healthcare facility at least once after testing on the mobile unit.
Linked to care (No)	A newly-diagnosed HIV+ individual who did not access HIV care at a public healthcare facility at least once after testing on the mobile unit.
PREDICTOR	**DEFINITION**
Presence of TB symptoms (Yes)	A newly-diagnosed HIV+ patient who had one or more TB symptoms (i.e. cough or fever for > 2 weeks, weight loss of > 1.5 kgs in the last month, drenching night sweats, loss of appetite, blood stained sputum) as documented by the nurse on the referral letter
Presence of TB symptoms (No)	A newly-diagnosed HIV+ patient who had none of the following TB symptoms (i.e. cough or fever for > 2 weeks, weight loss of > 1.5 kgs in the last month, drenching night sweats, loss of appetite, blood stained sputum), as documented by the nurse on the Tutu Tester client form.
Disclosed an HIV status (Yes)	A newly-diagnosed HIV+ patient who disclosed his/her HIV+ status to another individual as documented on the study questionnaire.
Disclosed an HIV status (No)	A newly-diagnosed HIV+ patient who did not disclosed his/her HIV+ status to another individual as documented on the study questionnaire.
Access to a cellphone (Yes)	A newly-diagnosed HIV+ patient who provided counselors with a cellphone number, as documented on the Tutu Tester locator form.
Access to a cellphone (No)	A newly-diagnosed HIV+ patient who did not provide counselors with a cellphone number, as documented on the Tutu Tester locator form.
Sex (Male)	A newly-diagnosed HIV+ patient who self-reported being male on the day of diagnosis, as documented on the Tutu Tester client form

Sex (Female)	A newly-diagnosed HIV+ patient who self-reported being female on the day of diagnosis, as documented on the Tutu Tester client form
Mean age	The average age of HIV+ patients on the day of diagnosis as documented on the Tutu Tester client form.
Age (≤30 years)	All newly-diagnosed HIV+ patients that were less than or equal to 30 years of age on the day of diagnosis, as documented on the Tutu Tester Client Form.
Age (≥ 31 years)	All newly-diagnosed HIV+ patients that were greater than or equal to 31 years of age on the day of diagnosis, as documented on the Tutu Tester Client Form.
Ever had an HIV test prior to testing at the mobile unit	A newly-diagnosed HIV+ patient that underwent HIV testing in the past before at an alternate testing facility, as documented on the Tutu Tester client form .
Mean laboratory CD4 count (cells/µl)	The average CD4 count of all newly-diagnosed HIV+ patients on the day of diagnosis, as documented on the laboratory result sheet.
Laboratory CD4 count CD4 ≤ 350 cells/µl	All newly-diagnosed HIV+ patients that had a baseline laboratory CD4 count result less than or equal to 350 cells/µl on the day of diagnosis, as documented on the laboratory result sheet.
Laboratory CD4 count CD4 > 350 cells/µl	All newly-diagnosed HIV+ patients that had a baseline laboratory CD4 count result greater than or equal to 351 cells/µl on the day of diagnosis, as documented on the laboratory result sheet.
WHO clinical stage (I vs. II, III and IV)	The clinical stage (I, II, III, IV) (as per WHO criteria) of a newly-diagnosed patient on the day of diagnosis, as documented on the Tutu Tester client form.
Mean BMI	The average body mass index (weight/height^2) of newly-diagnosed patients on the day of diagnosis, as documented on the Tutu Tester client form
Completed primary school (Yes)	A newly-diagnosed HIV+ patients who self-reported that he/she passed standard 5/grade 7, as documented on the study questionnaire
Completed primary school (No)	A newly-diagnosed HIV+ patients who self-reported that he/she did not go to primary school or did not pass/complete standard 5/grade 7, as documented on the study questionnaire
Employment status (Unemployed)	A newly-diagnosed HIV+ patient who self-reported that he/she does not have a job (part time, casual, full-time), as documented on the study questionnaire
Employment status (Employed)	A newly-diagnosed HIV+ patient who self-reported that he/she does have a job (part time, casual, full-time), as documented on the study questionnaire
Dwelling (Informal)	A newly-diagnosed HIV+ patient who self-reported that he/she lives in a dwelling that is constructed with tin/wood/cardboard, as documented on the study questionnaire.
Dwelling (Formal)	A newly-diagnosed HIV+ patient who self-reported that he/she lives in a dwelling with brick walls, cement/wooden floors, as documented on the study questionnaire.

Self-rating of health status (strong)	A newly-diagnosed HIV+ patient who self-reported that his/her current health was good/strong, as documented on the study questionnaire.
Self-rating of health status (average/weak)	A newly-diagnosed HIV+ patient who self-reported that his/her current health was fine/average or bad/weak, as documented on the study questionnaire.
Mean time (months) from diagnosis to accessing HIV care	The average time (months) between the date of a patient's HIV+ diagnosis and the date he/she enrolled in care at a health care facility, as documented on the study questionnaire.
On ART	A newly-diagnosed HIV+ patient with a baseline laboratory CD4 count <200 cells/ul that self-reported he/she accessed a health care facility and started ART, as documented on the study questionnaire.
Mean time (months) from accessing care to starting ART	The average time (months) between the date the newly-diagnosed ART-eligible patient (laboratory CD4 count <200 cells/ul) accessed care and the date he/she commenced ART, as documented on the study questionnaire.
Mean time (months) from diagnosis to starting ART	The average time (months) between the date the newly-diagnosed ART-eligible patient (laboratory CD4 count <200 cells/ul) was diagnosed and the date he/she commenced ART, as documented on the study questionnaire.
Scheduled to start ART	A newly-diagnosed ART-eligible patient (laboratory CD4 count <200 cells/ul) that did not commence ART, but was in the screening period and was a given a date to commence ART, as documented on the study questionnaire.