An audit of HIV Positive Patients Admitted to Helen Joseph Hospital in Johannesburg, South Africa

MMED Proposal

Department of Internal Medicine

University of the Witwatersrand, Johannesburg, South Africa

Investigator: Dr Gregory Saul Yudelowitz
Student Number: 302891
Degree: Mmed Internal Medicine

Supervisors:

1. Professor Prudence Ive: Division of Infectious Diseases, Department of Internal Medicine, Helen Joseph Hospital
2. Professor Matthew Fox: Department of Epidemiology and Global Health, Boston University

DECLARATION

I, Gregory Yudelowitz declare that this Research Report is my own, unaided work. It is being submitted for the degree of Master of Medicine in the department of internal medicine at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at any other university.

Signature:  **……**

Date: **……22/05/2020……**

Place: **……Johannesburg……**

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

FACULTY OF HEALTH SCIENCES

PLAGIARISM DECLARATION TO BE SIGNED BY ALL HIGHER DEGREE STUDENTS

SENATE PLAGIARISM POLICY: APPENDIX ONE

I GREGORY SAUL YUDELOWITZ (Student number: 302891) am a student registered for the degree of MMED in the academic year 2019.

I hereby declare the following:

- I am aware that plagiarism (the use of someone else's work without their permission and/or without acknowledging the original source) is wrong.
- I confirm that the work submitted for assessment for the above degree is my own unaided work except where I have explicitly indicated otherwise.
- I have followed the required conventions in referencing the thoughts and ideas of others.
- I understand that the University of the Witwatersrand may take disciplinary action against me if there is a belief that this is not my own unaided work or that I have failed to acknowledge the source of the ideas or words in my writing.
- I have included as an appendix a report from "Turnitin" (or other approved plagiarism detection) software indicating the level of plagiarism in my research document.

Signature: _____ Date: 10/10/2019

Acknowledgments

I would like to express thanks to the following people without whom I could not have completed this research report:

To my supervisors: Professor Prudence Ive and Professor Mathew fox. You both guided me through this process every step of the way and were always readily available for encouragement. Your swift responses to my many questions were much appreciated. Thank you for the excellent guidance and advice.

To my family: Thank you for putting up with the constant chatting and questions about the research report and process.

Most importantly thank you to my wife Gabi, for her never ending support and encouragement in assisting me with this research.

Abstract

Background

South Africa has the largest HIV infected population and treatment programme in the world. ART access has increased since 2004 with the current policy of universal test and treat. South Africa has had some success toward the UNAIDS 90-90-90 targets but high numbers of HIV related complications and treatment failure persist despite universal access to ART. The aim of this study was to estimate the proportion of patients being admitted to medical wards that are HIV infected and to calculate the median CD4 count for these patients.

Methods

A prospective descriptive study in which baseline data was collected from medical patients admitted to Helen Joseph Hospital, in Johannesburg from September 2018 to January 2019. The number of HIV infected admissions was assessed and median CD4 count and viral load was calculated. Reasons for admission among HIV infected and non-infected patients were compared.

Results

The median CD4 cell count for HIV positive admissions was 67 cells/µl (IQR 23-259.5) 42.4% of 794 medical admissions were HIV infected. Over a quarter of HIV-related admissions were newly diagnosed on admission. 46.1% of patients on treatment were failing ART. More than 10% of HIV-infected patients had interrupted treatment with a similar number of patients previously known to be HIV infected having not yet initiated treatment. AIDS defining conditions accounted for more than 40% of reasons for admission.

Conclusion

Median CD4 counts remain low in hospitalised HIV positive patients despite universal access to ART. Large numbers of HIV patients are not accessing or are disengaging from HIV care.

Table of Contents

List of Tables

List of Figures

List of Abbreviations

AIDS	**Acquired Immune Deficiency Syndrome**
ART	**Anti retro viral therapy**
FDC	**Fixed dose combination**
HIV	**Human Immunodeficiency virus**
LAM	**Lipoarabinomanann**
NCD	**Non-communicable disease**
PMTCT	**Prevention of Mother to Child Transmission**
STI	**Sexually Transmitted Infections**
TB	**Tuberculosis**
UNAIDS	**Joint United Nations Programme on HIV and AIDS**

CHAPTER ONE: PROTOCOL WITH EXTENDED LITERATURE REVIEW

1.1 Introduction

South Africa has the largest Human Immunodeficiency Virus (HIV) epidemic in the world and therefore suffers a large part of the global burden of the HIV and Acquired Immune Deficiency Syndrome (AIDS) pandemic (1). South Africa has 19% of the worldwide population of people living with HIV infection, 15% of new infections and 11% of AIDS related deaths (1). According to the Joint United Nations Programme on HIV and AIDS (UNIADS) South Africa had 270 000 new HIV infections and 110 000 AIDS-related deaths in 2016. There were more than 7 million people living with HIV infection, with just over a half of that number accessing antiretroviral therapy (ART) (1). Less than half of the people living with HIV infection had suppressed viral loads. Since 2010, new HIV infections declined by 49% and AIDS-related deaths have dropped by 29%. South Africa has the largest antiretroviral treatment programme in the world, accounting for a fifth of people on antiretroviral therapy worldwide (1).

The United Nations Sustainable Development Goals for Health aim to end the HIV epidemic by 2030 (2). To obtain this goal, UNAIDS developed a plan known as “90 90 90” (2). This being that 90 percent of all people living with HIV will know their HIV status, 90 percent of HIV infected individuals will receive ART and 90 percent of patients on ART will have HIV viral suppression by 2020. In summary 90% diagnosed, 90% treated, and 90% suppressed. Some European countries may be close to that target (3). However much of the developing world, especially sub-Saharan Africa, is still lagging behind despite the expansion in access to care (1, 3, 4).

Since 2004 there has been a substantial increase in access to ART in South Africa with numerous changes to National guidelines and expansions in ART eligibility from an initial threshold of a CD4 count less than 200 cells/µl at the start of the treatment rollout (4). Strategies that have been used to curb the epidemic include the use of fixed-dose combination pills (FDC) to improve adherence and retention, as well as the expansion of The Prevention of Mother to Child Transmission (PMTCT) program to provide lifelong ART to all pregnant and breastfeeding woman regardless of CD4

cell counts or clinical staging (5).The country has undergone numerous policy changes and developed strategies to try and tackle the extensive burden of disease (4), with the most recent strategy being announced at the end of 2016 with new guidelines developed to initiate all people with HIV infection on ART regardless of CD4 cell counts (6). South Africa has also recently launched The National Strategic Plan for HIV, Tuberculosis (TB) and Sexually Transmitted Infections(STIs) 2017–2022 aiming to reduce new HIV infections, improve treatment, care and support, and expand access to key and vulnerable populations, and develop ways to change the social and structural drivers of HIV, tuberculosis and sexually transmitted infections (1).

Numerous factors have altered the course of the HIV pandemic within South Africa. ART has shown an impact with a vast decline in mortality in the last 20 years (7). Results from the STRETCH trial (Streamlining Tasks and Roles to Expand Treatment and Care for HIV) showed that nurse-centred treatment was not inferior to doctor-managed care (8). Strategies such as task shifting, which involves the extension to primary-care nurses' roles to include ART initiation, and decentralization of HIV treatment can be done safely, and improve health outcomes and quality of care. These strategies have provided ways to deal with the growing number of patients requiring treatment (9). It has been suggested that these strategies could increase patient compliance, decrease interruption rates and loss to follow up as well as lessen the patient load at referral hospitals (9).

Despite these strategies South Africa is still struggling to achieve the “90 90 90” targets. Within South Africa, before the rollout of ART, up to half of medical admissions to state hospitals were HIV related (10, 11). From June 2012 to October 2013, almost a decade into the ART era in the country, over 60 percent of all medical admissions in a district hospital in Cape Town, South Africa, were HIV-related (12). Up to 15 percent of the HIV infected patients, at the same hospital, were newly diagnosed on admission and nearly a quarter of those known to be HIV infected prior to admission were ARV naïve. Mortality rates were up to 13 percent amongst the HIV infected patients within a three month period and one third of the patients required readmission to hospital within the same time frame (12). Clinical and laboratory characteristics have been shown to identify those at risk for increased

mortality. These include significant weight loss, symptoms such as fever and vomiting, impairment of activities of daily living and grip strength (13).Almost 20 percent of the HIV infected patients had previously been exposed to ART and among those on ART nearly 50 percent were not virologically suppressed. Interestingly using the virological failure threshold as 400 instead of 1000 copies/ml did not change the proportion of treatment success (14). Of note is that up to a quarter of the HIV patients were suppressed on ART but still developed conditions requiring hospitalisation (12). This may be due to the fact that in lower income settings, patients are initiating ART at low CD4 cell counts (15) and are thus still susceptible to opportunistic infections.

A relatively recent systematic review and meta-analysis has shown that HIV-AIDS associated diseases, predominantly TB, and bacterial infections were the most common causes of HIV related admissions worldwide and accounted for the majority of mortality (16). Other HIV associated infections resulting in admission were oral candidiasis, *Pneumocystis Jirovecii* pneumonia and central nervous system toxoplasmosis. The same review noted that reduced CD4 cell counts on hospital admission were associated with TB infection as the reason for admission as well as increased length of stay in hospital (16). In Cape Town, similar trends were found with TB and bacterial infections again being the most common causes for admission, with other AIDS-defining illnesses (opportunistic infections and AIDS-related malignancies) being the next most common (12).

Even with the strategies implemented, such as task shifting and decentralization, programs are struggling to cope with the HIV burden in South Africa (10, 12). Hospitals are still seeing the complications of advanced HIV infection in an era when there is supposedly access to ART for all those living with HIV infection (10). A study conducted in Johannesburg, South Africa, at a regional public sector hospital found that nearly half of the medical admissions were known to be HIV infected. In addition mortality rates were higher amongst the HIV infected patients (10). The median CD4 cell count for these patients was 90 cells/µl (10). At Groote Schuur Hospital in Cape Town, South Africa, a tertiary medical institution, up to half of the HIV infected patients admitted to the Infectious disease unit were ARV naïve and the mean CD4 count of all the HIV infected patients was only 128 cells/µl (17). HIV infected patients

requiring admission to the Intensive care Unit at the same hospital had a median CD4 of 232.5 cellsμ/l and a mean HIV Viral Load of 2 218 556.5 RNA copies/mL (18). More than half of these patients were not on ART and of those already on ART the mean duration of treatment was only 6.3 months (18). At a different hospital in Cape Town, patients newly diagnosed on admission to general medical wards had a median CD4 cell count of 73 cells/μl and the median CD4 count amongst patients having interrupted ART was 71 cells/μl (12).

The situation in the rest of Sub-Saharan Africa shows little difference . CD4 cell counts at patient presentation and at ART initiation have not changed substantially in more than a decade despite making ART available to millions of HIV infected people. Mean CD4 counts at presentation are still under 300 cells/μl, while those at ART initiation are under 200 cells/μl (19). Low CD4 counts are also a predictor of risk for readmission (20).

With numerous strategies in place, and treatment regardless of CD4 count, it would be expected that baseline CD4 counts should rise (21).However 16 years into a sustained and comprehensive treatment plan, South Africa may still be experiencing high rates of treatment failure, loss to follow up and discontinuation of treatment and therefore not achieving the benefits of ART (22). In this era of 'Test and Treat' HIV associated conditions and complications would also be expected to have declined, however they remain substantial (23) with a significant number of HIV infected patients are still presenting with complications of HIV.

South Africa is facing complex challenges that could undermine achieving the 90 90 90 goals. Geographic and transportation related barriers, HIV associated stigma and poverty are some of the issues hampering the countries response to the pandemic (24). HIV testing is still not reaching some areas in South Africa resulting in late presentations followed by the associated complications (3, 25).

There is a decreasing proportion of patients presenting newly diagnosed with advanced HIV showing some success in the universal test and treat policy (26). However patients are lost to follow up due to a combination of reasons. Factors associated with loss to follow up have been found to include younger age (less than

30 years), male gender and pregnancy at the initiation of ART (27). Interestingly higher CD4 counts at ART initiation have also been associated with disengagement of care (28). Another important contributing factor of loss to follow up is to a lack of tracking processes (25). Patients are continuously initiating ART at low CD4 cell counts and AIDS defining opportunistic infections are persisting (12, 16). Contributing factors to early mortality are patient attrition and delayed collection of treatment (29).

Retention in care plays a vital role in meeting the UNAIDS “90 90 90” target. Patients’ disengaging from care is thus an important challenge. A recent study in Cape Town, South Africa, showed that up to 23% of patients on ART disengaged from care at least once in a 2 year period (27). It is important to bear in mind that this study was done in a well-established ART centre and still suffered from large rates of loss to follow up therefore highlighting the more drastic situation in less well-established ART centres. Patients lost to follow up not only do not benefit from ART but put further strain on an already under resourced and overworked health system by transmitting HIV to uninfected individuals, developing opportunistic infections and developing drug resistance thus further undermining the UNAIDS goal (27). Factors predicting retention in care were a baseline CD4 cell count of less than 350 cells/µl as well as being a member of an adherence support club thus possibly suggesting a way forward to curb this problem (27). Additional reasons for these failures may be recent HIV diagnosis, refusal of patients to take ART and previous ineligibility based on old guidelines (12). Further techniques used to improve the ART programme performance are more rapid ART initiation, more efficient interrupter re-initiation, the newer fixed dose antiretrovirals decreasing pill burden and newer drugs with improved side effect profiles (25). Of note, same day initiation of ART has shown promise in retention in care especially to groups of young men and those patients who attend primary care clinics (30). Another concerning issue hampering the success of universal treatment is that some patients are not initiating treatment at all (31).This is due to a number of factors including patient factors such as stigma, costs of travel to and from clinics and heath care provider factors such as stock outs, long waiting times, staff shortage and inadequate communication between health professionals and patients (31). If patients eligible for ART do not initiate treatment then treatment regardless of CD4 count cannot have the desired impact (31, 32).

This highlights the fact that there are still major pitfalls in the cascade of care targeting the HIV epidemic within South Africa. An increasing concern is that a decrease in the number of patients presenting with advanced HIV due to early treatment, may now be countered by a rising proportion of patients already on ART but who have either interrupted or failed therapy (26). At the time of writing the author is unaware of any research studying the trends of HIV infected patients in tertiary hospitals in Johannesburg, South Africa, where it is perceived that many patients are presenting newly diagnosed on admission, interrupting or failing treatment. As mentioned above, a study conducted in 2010 within Johannesburg, found that up to half of medical admissions were HIV infected with a median CD4 count of 90 cells/µl. This was during the time when the threshold for ART initiation was a CD4 count of 200 cells/µl and is now out of date with the current guidelines (10). This together with the challenges faced, makes it vital to identify these trends, within the current environment of treating HIV regardless of treating CD4 counts, in order to develop strategies to combat the expanding pandemic and come closer to the UNAIDS goals.

1.2 Aim

The aims of this study are to describe the epidemiology of HIV infection, to determine the reasons for hospital admissions among HIV infected patients, to estimate the proportion of medical patients being admitted to general medical wards that are HIV infected and to calculate the median CD4 count for these patients to be used as a marker of the current situation of the HIV pandemic, all within a tertiary hospital setting, almost 15 years into the ART era.

1.3 Objectives

- To determine the percentage of patients with medical admissions who are HIV infected and not infected
- To identify the demographic characteristics of HIV infected patients
- To describe the ART history and laboratory characteristics of the HIV infected patients within a tertiary hospital setting

- To describe reasons for admission and co morbid diseases among HIV infected patients compared to HIV uninfected patients

1.4 Research Methodology

1.4.1 Study Population

All medical patients admitted by a single medical unit during general medical intakes at Helen Joseph Hospital from September 2018 to March 2019

1.4.2 Sample size

Patient numbers to be obtained for the study:

- Helen Joseph Hospital: maximum 800 patients

These numbers are based on the average number of patients seen by a Medical Registrar, with 3 to 4 registrars per medical unit, at Helen Joseph hospital over a three-month period with approximately 5 intakes of patients per month per registrar.

1.4.3 Study Design

The study design was a descriptive study. Data was collected from patients as they were admitted to the general medical wards. No personal identification details of patients will be revealed in this study. Patients will remain anonymous. Results of tests from patient's medical records were used. These tests were only done if required as part of routine standard of patient care (or previously done) and no additional and unnecessary tests were conducted and no additional costs were incurred by the hospital. Data was collected during the medical intakes for all patients admitted by one medical unit. Only baseline data on admission was recorded. Data was collected from Helen Joseph Hospital from November 2018 to March 2019.

HIV infected patient's viral load and CD4 results were obtained from the National Health Laboratory Service (NHLS) Labtrack system if these tests are taken as part of their care during admission. Only medical records of patients were used. If found to be HIV infected, the results were used but no names or identifiable numbers were recorded. CD4 counts were recorded only if required during their inpatient care.

1.4.4 Data collected:

Demographics

- Gender
- Age
- Occupation

ART history and laboratory characteristics

- If ARV naïve/ on Treatment/ interrupted ART
- Reasons for interrupting ART
- CD4 count
- Viral load

Reasons for admission and comorbid diseases

- TB
- Other HIV associated infections
- Bacterial Infections
- AIDS-defining malignancies
- Drug related conditions (adverse reactions and overdose)
- Non-communicable diseases and associated complications(Diabetes mellitus, Hypertension, heart failure, Chronic Obstructive Pulmonary Disease)
- Renal dysfunction
- Liver dysfunction
- Central nervous system disorders : strokes/ seizures
- Thrombo-embolic disease
- Psychiatric illnesses

See Appendix 1: Data Collection Table

1.4.5 Research assumptions

Virological failure will be defined as per the World Health Organisation (WHO) definition: Plasma viral load above 1000 copies/ mL based on two consecutive viral load measurements after 3 months, with adherence support (33).

Interruption of treatment will be defined as stopping treatment for more than 5 days. ARV naïve defined as patients known to be HIV positive not yet on ART.

1.4.6 Management of Patient Data

Data obtained from patient records will be transferred to an Excel 2007 datasheet (Microsoft, USA).This document will be password protected and access limited only to the author and supervisors (Appendix 1).

1.5 Data Analysis

Data will be evaluated using descriptive statistics. Normal distribution will be represented by means and standard deviation. Skewed distributions will be shown by medians and interquartile ranges.

1.5.1 Key variables to be measured will be CD4 counts of all HIV infected patients and comparing CD4 counts of newly diagnosed HIV infected patients, known HIV patients that are ARV naïve(patients who have never initiated ART) and those patients on treatment (on ART) including those who have interrupted. Median CD4 counts will then be used as an indication of the progress made in the HIV cascade of care within Tertiary Hospitals in Johannesburg.

1.5.2 A comparison will be made between the median CD4 counts calculated in this study to the values found in earlier studies in Cape Town (12), mentioned in the introduction. The median CD4 count from this study is predicted to be higher as the study is being conducted at a tertiary level hospital compared to that of a district hospital, as well as the fact that it will be conducted during a time off access to ART for all HIV infected patients. Further comparisons will be made between Median CD4 counts of those patients found to be newly diagnosed HIV infected on admission, those already on ART and patients who have interrupted ART. Additionally the results from male and female patients will be compared as well as those of different age groups. The age groups to be compared will be 18 years of age to 35 years, 35 to 50 years and 50 years and older.

1.5.3 Confounding variables identified that may impact results would be illnesses that affect CD4 cell counts, such as Syphilis and Systemic Lupus Erythematosus (34, 35), thereby impacting on the overall median CD4 cell count calculated.

1.6 Ethical considerations

Ethics approval was obtained from the CEO office and research committee at Helen Joseph Hospital as well as the University of Witwatersrand Human Research Ethics Committee (Medical) for the research to be conducted (Appendix 3.5). Only results of tests that patients have consented to as part of their routine inpatient care were used. The information was be anonymized and only the author had access to the results by reviewing medical records. No blood samples were collected specifically for this study, only biomedical and clinical data from tests conducted as part of routine care were extracted from existing records that are routinely collected at the study sites as part of routine patient care. The study therefore posed no physical risks to patients

Potential risks of accidental disclosure of patient's HIV status and loss of confidentiality

A possible risk is loss of confidentiality. Data being collected will indicate individuals' HIV status. HIV stigma continues to be a major factor among patients and hinders the disclosure of HIV status. This risk will be protected against by the fact that no patients' identifiers will be collected and a master list of data will be stored in a password protected document. Data will be captured on site and therefore no written records containing identifiers will leave the study sites.

Informed Consent

As mentioned above, no blood samples will be drawn specifically for the purpose of this study. HIV testing, and any further tests required as part of routine patient care, will only be done after adequate counselling and informed consent in accordance with the National Department of Health Guidelines. Participating patients will be given an information sheet (Appendix 2) before signing an informed consent form (Appendix 3) prior to any of their records being used or data collected.

1.7 Timing

	Jan	Feb	March	Apr	May	June	July	Aug	Sept	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	Jun
Literature Review																		
Preparing protocol																		
Protocol assessment																		
Ethics application																		
Collecting Data																		
Data Analysis																		
Writing up paper																		

1.8 Funding

No external funding will be required for the research. Minimal costs are expected while conducting this research and therefore no funding will be requested.No additional costs will be placed on the partaking hospital as test results being used will only be those used as part of routine standard of patient care. No additional tests will be requested. The costs of printing will be covered individually by the author.

1.9 Potential Study Limitations

Anticipated problems to arise:

- ❖ Patients declining HIV testing resulting in incomplete data collection.
- ❖ Record Keeping:
  - Difficulty finding results for patients due to incorrect patient's details entered on NHLS Labtrack system.
  - Missing data from patient medical records
- ❖ Limited Confounder adjustment data (the study does not adjust for other causes of a deceased CD4 cell count)
- ❖ Incorrect admission diagnosis resulting in inaccurate data on reasons for admission.
- ❖ Short time period for collecting data possibly resulting in low patients numbers for study.

1.10 References

1. South Africa | UNAIDS [Internet]. [Cited 2018 Mar 14]. Available from: http://www.unaids.org/en/regionscountries/countries/southafrica
2. 90–90–90 - An ambitious treatment target to help end the AIDS epidemic | UNAIDS [Internet]. [cited 2019 Sep 6]. Available from: https://www.unaids.org/en/resources/documents/2017/90-90-90
3. Darling KE, Hachfeld A, Cavassini M, Kirk O, Furrer H, Wandeler G. Late presentation to HIV care despite good access to health services: current epidemiological trends and how to do better. Swiss Med Wkly [Internet]. 2016 Aug 21 [cited 2018 Mar 14];146:w14348. Available from: http://doi.emh.ch/smw.2016.14348
4. Katz IT, Kaplan R, Fitzmaurice G, Leone D, Bangsberg DR, Bekker L-G, Orrell C. Treatment guidelines and early loss from care for people living with HIV in Cape Town, South Africa: A retrospective cohort study. Deeks SG, editor. PLoS Med [Internet]. 2017 Nov 14 [cited 2018 Mar 14];14(11):e1002434. Available from: http://dx.plos.org/10.1371/journal.pmed.1002434
5. South African Department of Health. National consolidated guidelines for theprevention of mother-to-child transmission of HIV (PMTCT) and the management of HIV in children, adolescents and adults 24 December 2014 (cited 2018 January 21) http://www.kznhealth.gov.za/family/HIV-Guidelines-Jan2015.pdf
6. Meintjes G, Moorhouse MA, Carmona S, N Davies, S Dlamini, C Van Vuuren, T Manzini, M Mathe, Y Moosa J Nash, J Nel, Y Pakade, J Woods, G Van Zyl, F Conradie, F Venter. Adult antiretroviral therapy guidelines 2017. S Afr J HIV Med. 2017;18(1), a776. https://doi.org/10.4102/ sajhivmed.v18i1.776

7. Bor J, Herbst AJ, Newell M-L, Bärnighausen T. Increases in adult life expectancy in rural South Africa: valuing the scale-up of HIV treatment. Science [Internet]. 2013 Feb 22 [cited 2018 Mar 14];339(6122):961–5. Available from: http://www.sciencemag.org/cgi/doi/10.1126/science.1230413
8. Fairall L, Bachmann MO, Lombard C, Timmerman V, Uebel K, Zwarenstein M,Boulle A, Georgeu D,Colvin C, Lewin S, Faris G,Cornick R, Draper B, Tshabalala M, Kotze E,van Vuuren C, Steyn D, Chapman R, Bateman E. Task shifting of antiretroviral treatment from doctors to primary-care nurses in South Africa (STRETCH): a pragmatic, parallel, cluster-randomised trial. Lancet [Internet]. 2012 Sep 8 [cited 2018 Mar 15];380(9845):889–98. Available from: http://www.ncbi.nlm.nih.gov/pubmed/22901955
9. Grimsrud A, Kaplan R, Bekker L-G, Myer L. Outcomes of a nurse-managed service for stable HIV-positive patients in a large South African public sector antiretroviral therapy programme. Trop Med Int Heal [Internet]. 2014 Sep [cited 2018 Mar 14];19(9):1029–39. Available from: http://doi.wiley.com/10.1111/tmi.12346
10. Long LC, Fox MP, Sauls C, Evans D, Sanne I, Rosen SB. The High Cost of HIV-Positive Inpatient Care at an Urban Hospital in Johannesburg, South Africa. Fischer G, editor. PLoS One [Internet]. 2016 Feb 17 [cited 2018 Mar 14];11(2):e0148546. Available from: http://dx.plos.org/10.1371/journal.pone.0148546
11. Colvin M, Dawood S, Kleinschmidt I, Mullick S, Lallo U. Prevalence of HIV and HIV-related diseases in the adult medical wards of a tertiary hospital in Durban, South Africa. Int J STD AIDS [Internet]. 2001 Jun 25 [cited 2018 Mar 14];12(6):386–9. Available from: http://journals.sagepub.com/doi/10.1258/0956462011923336
12. Meintjes G, Kerkhoff AD, Burton R, Schutz C, Boulle A, Van Wyk G, et al. HIV-Related Medical Admissions to a South African District Hospital Remain Frequent Despite Effective Antiretroviral Therapy Scale-Up. Medicine (Baltimore) [Internet]. 2015 Dec [cited 2018 Mar 14];94(50):e2269. Available from: https://insights.ovid.com/crossref?an=00005792-201512150-00045
13. Siika A, McCabe L, Bwakura-Dangarembizi M, Kityo C, Mallewa J, Berkley J, Maitland K, Griffiths A, Baleeta K, Mudzingwa S, Abach J, Nathoo K, Thomason M, Prendergast A, Walker A, Gibb D. Late Presentation With HIV

in Africa: Phenotypes, Risk, and Risk Stratification in the REALITY Trial. Clin Infect Dis [Internet]. 2018 Mar 4 [cited 2019 Apr 12];66(suppl_2):S140–6. Available from: http://www.ncbi.nlm.nih.gov/pubmed/29514235

14. Taieb F, Madec Y, Cournil A, Delaporte E. Virological success after 12 and 24 months of antiretroviral therapy in sub-Saharan Africa: Comparing results of trials, cohorts and cross-sectional studies using a systematic review and meta-analysis. PLoS One [Internet]. 2017 [cited 2019 Apr 12];12(4):e0174767. Available from: http://www.ncbi.nlm.nih.gov/pubmed/28426819
15. Avila D, Althoff KN, Mugglin C, Wools-Kaloustian K, Koller M, Dabis F, Nash D, Gsponer T, Sungkanuparph S, McGowan C, May M, Cooper D, Chimbetete C, Wolff M, Collier A, McManus H, Davies MA, Costagliola D, Crabtree-Ramirez B, Chaiwarith R, Cescon A, Cornell M, Diero L, Phanuphak P, Sawadogo A, Ehmer J, Eholie SP, Li PC, Fox MP, Gandhi NR, González E, Lee CK, Hoffmann CJ, Kambugu A, Keiser O, Ditangco R, Prozesky H, Lampe F, Kumarasamy N, Kitahata M, Lugina E, Lyamuya R, Vonthanak S, Fink V, d'Arminio Monforte A, Luz PM, Chen YM, Minga A, Casabona J, Mwango A, Choi JY, Newell ML, Bukusi EA, Ngonyani K, Merati TP, Otieno J, Bosco MB, Phiri S, Ng OT, Anastos K, Rockstroh J, Santos I, Oka S, Somi G, Stephan C, Teira R, Wabwire D, Wandeler G, Boulle A, Reiss P, Wood R, Chi BH, Williams C, Sterne JA, Egger M., . Immunodeficiency at the start of combination antiretroviral therapy in low-, middle- and high-income countries. JAIDS J Acquir Immune Defic Syndr [Internet]. 2013 Jul 1 [cited 2018 Mar 14];65(1):1. Available from: http://www.ncbi.nlm.nih.gov/pubmed/24419071
16. Ford N, Shubber Z, Meintjes G, Grinsztejn B, Eholie S, Mills EJ, et al. Causes of hospital admission among people living with HIV worldwide: a systematic review and meta-analysis. Lancet HIV [Internet]. 2015 Oct [cited 2018 Mar 14];2(10):e438–44. Available from: http://www.ncbi.nlm.nih.gov/pubmed/26423651
17. Pandie M, Van der Plas H, Maartens G, Mendelson M. The role of the infectious diseases unit at Groote Schuur Hospital in addressing South Africa's greatest burden of disease. S Afr Med J [Internet]. 2012 May 23 [cited 2018 Mar 14];102(6):528–31. Available from: http://www.ncbi.nlm.nih.gov/pubmed/22668956

18. Mkoko P, Raine RI. HIV-positive patients in the intensive care unit: A retrospective audit. S Afr Med J [Internet]. 2017 Sep 22 [cited 2018 Mar 14];107(10):877–81. Available from: http://www.ncbi.nlm.nih.gov/pubmed/29022532
19. Siedner MJ, Ng CK, Bassett I V., Katz IT, Bangsberg DR, Tsai AC. Trends in CD4 Count at Presentation to Care and Treatment Initiation in Sub-Saharan Africa, 2002-2013: A Meta-analysis. Clin Infect Dis [Internet]. 2014 Dec 16 [cited 2018 Mar 14];60(7):1120–7. Available from: http://www.ncbi.nlm.nih.gov/pubmed/25516189
20. Nijhawan AE, Clark C, Kaplan R, Moore B, Halm EA, Amarasingham R. An electronic medical record-based model to predict 30-day risk of readmission and death among HIV-infected inpatients. J Acquir Immune Defic Syndr [Internet]. 2012 Nov 1 [cited 2018 Mar 14];61(3):349–58. Available from: http://content.wkhealth.com/linkback/openurl?sid=WKPTLP:landingpage&an=00126334-201211010-00014
21. Cornell M, Johnson LF, Wood R, Tanser F, Fox M, Prozesky H, Schomaker M, Egger M, Davies M, Boulle A . Twelve-year mortality in adults initiating antiretroviral therapy in South Africa. J Int AIDS Soc [Internet]. 2017 [cited 2019 Apr 12];20(1):21902. Available from: http://www.ncbi.nlm.nih.gov/pubmed/28953328
22. Plazy M, Dabis F, Naidu K, Orne-Gliemann J, Barnighausen T, Dray-Spira R. Change of treatment guidelines and evolution of ART initiation in rural South Africa: data of a large HIV care and treatment programme. BMC Infect Dis [Internet]. 2015 Oct 26 [cited 2018 Mar 14];15(1):452. Available from: http://bmcinfectdis.biomedcentral.com/articles/10.1186/s12879-015-1207-2
23. Gabillard D, Lewden C, Ndoye I, Moh R, Segeral O, Tonwe-Gold B, Etard J-F,Pagnaroat M, Fournier-Nicolle I,Eholié S,Konate I,Minga A,Mpoudi-Ngolé E,Koulla-Shiro S, Zannou D, Anglaret X, Laurent C. Mortality, AIDS-morbidity, and loss to follow-up by current CD4 cell count among HIV-1-infected adults receiving antiretroviral therapy in Africa and Asia: data from the ANRS 12222 collaboration. J Acquir Immune Defic Syndr [Internet]. 2013 Apr 15 [cited 2019 Apr 16];62(5):555–61. Available from: http://www.ncbi.nlm.nih.gov/pubmed/23274931

24. Larson BA, Brennan A, McNamara L, Long L, Rosen S, Sanne I, Fox M. Early loss to follow up after enrolment in pre-ART care at a large public clinic in Johannesburg, South Africa. Trop Med Int Health 2010,15 Suppl 1:43–47. pmid:20586959
25. Venter WDF, Ford N, Vitoria M, Stevens W. Diagnosis and monitoring of HIV programmes to support treatment initiation and follow up and improve programme quality. Curr Opin HIV AIDS [Internet]. 2017 Mar [cited 2018 Mar 14];12(2):117–22. Available from: http://www.ncbi.nlm.nih.gov/pubmed/28134712
26. Osler M, Hilderbrand K, Goemaere E, Ford N, Smith M, Meintjes G, Kruger J, Govender N, Boulle A. The Continuing Burden of Advanced HIV Disease Over 10 Years of Increasing Antiretroviral Therapy Coverage in South Africa. Clin Infect Dis [Internet]. 2018 Mar 4 [cited 2019 Apr 12];66(suppl_2):S118–25. Available from: http://www.ncbi.nlm.nih.gov/pubmed/29514233
27. Kaplan SR, Oosthuizen C, Stinson K, Little F, Euvrard J, Schomaker M, et al. Contemporary disengagement from antiretroviral therapy in Khayelitsha, South Africa: A cohort study. Newell M-L, editor. PLoS Med [Internet]. 2017 Nov 7 [cited 2018 Mar 14];14(11):e1002407. Available from: http://dx.plos.org/10.1371/journal.pmed.1002407
28. Grimsrud A, Cornell M, Schomaker M, Fox MP, Orrell C, Prozesky H, et al. CD4 count at antiretroviral therapy initiation and the risk of loss to follow-up: results from a multicentre cohort study. J Epidemiol Community Health [Internet]. 2016 Jun [cited 2018 Mar 14];70(6):549–55. Available from: http://jech.bmj.com/lookup/doi/10.1136/jech-2015-206629
29. Fox MP, Rosen S. Retention of Adult Patients on Antiretroviral Therapy in Low- and Middle-Income Countries: Systematic Review and Meta-analysis 2008-2013. J Acquir Immune Defic Syndr [Internet]. 2015 May 1 [cited 2019 Apr 16];69(1):98–108. Available from: http://www.ncbi.nlm.nih.gov/pubmed/25942461
30. Rosen S, Maskew M, Fox MP, Nyoni C, Mongwenyana C, Malete G, Sanne I, Bokaba D, Sauls C, Rohr J, Long L. Initiating Antiretroviral Therapy for HIV at a Patient's First Clinic Visit: The RapIT Randomized Controlled Trial. PLOS

Med [Internet]. 2016 Jun 3 [cited 2018 Mar 14];13(6):e1002050. Available from: http://www.ncbi.nlm.nih.gov/pubmed/27258028

31. Bor J, Chiu C, Ahmed S, Katz I, Fox MP, Rosen S, Yapa M, Tanser F, Pillay D, Bärnighausen T. Failure to initiate HIV treatment in patients with high CD4 counts: evidence from demographic surveillance in rural South Africa. Trop Med Int Health [Internet]. 2018 [cited 2019 Apr 12];23(2):206. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5829292/
32. Bor J, Ahmed S, Fox MP, Rosen S, Meyer-Rath G, Katz IT, Tanser F, Pillay D, Bärnighausen T. Effect of eliminating CD4-count thresholds on HIV treatment initiation in South Africa: An empirical modeling study. PLoS One [Internet]. 2017 [cited 2019 Apr 16];12(6):e0178249. Available from: http://www.ncbi.nlm.nih.gov/pubmed/28617805
33. Who.int. 2018 [cited 30 January 2018]. Available from: http://www.who.int/hiv/pub/guidelines/arv2013/art/WHO_CG_table_7.15.pdf
34. Ferreira S, Vasconcelos J, Marinho A, Farinha F, Almeida I, Correia J, Barbosa P, Mendonça T, Vasconcelos C. [CD4 lymphocytopenia in systemic lupus erythematosus]. Acta Reumatol Port [Internet]. [cited 2018 Mar 18];34(2A):200–6. Available from: http://www.ncbi.nlm.nih.gov/pubmed/19474774
35. Palacios R, Jiměnez-Oñate F, Aguilar M, Galindo MJ, Rivas P, Ocampo A, Berenguer J, Arranz JA, Ríos MJ, Knobel H, Moreno F, Ena J, Santos J. Impact of Syphilis Infection on HIV Viral Load and CD4 Cell Counts in HIV-Infected Patients. JAIDS J Acquir Immune Defic Syndr [Internet]. 2007 Mar 1 [cited 2018 Mar 18];44(3):356–9. Available from: http://www.ncbi.nlm.nih.gov/pubmed/17159654

CHAPTER 2: SUBMISSIBLE ARTICLE

An audit of HIV infected Patients Admitted to Helen Joseph Hospital in Johannesburg, South Africa

Authors:

Gregory Yudelowitz , MBBCh (wits), Dip HIV Man (SA)

Prudence Ive, MBBCh, FCP, Cert ID Phys
Mathew P Fox, DSc, MPH

Affiliations:
Division of Infectious Diseases, Department of Internal Medicine, Helen Joseph Hospital, Johannesburg
School of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa
Boston University School of Public Health, Boston University, Boston, MA, USA

Conflicts of interest: None

Key words: Median CD4 count, inpatient, , South Africa, HIV, TB, reasons for admission, reason for treatment interruption

Corresponding author:

Gregory Yudelowitz

Mobile number: 0836846493

Email: gregyudels@gmail.com

Abstract word count: 244 **Total word count:** 3284

Abstract

Background

South Africa has the largest HIV infected population and treatment programme in the world. ART access has increased since 2004 with the current policy of universal test and treat. South Africa has had some success toward the UNAIDS 90-90-90 targets but high numbers of HIV related complications and treatment failure persist despite universal access to ART. The aim of this study was to estimate the proportion of patients being admitted to medical wards that are HIV infected and to calculate the median CD4 count for these patients.

Methods

A prospective descriptive study in which baseline data was collected from medical patients admitted to Helen Joseph Hospital, in Johannesburg from September 2018 to January 2019. The number of HIV infected admissions was assessed and median CD4 count and viral load was calculated. Reasons for admission among HIV infected and non-infected patients were compared.

Results

The median CD4 cell count for HIV positive admissions was 67 cells/µl (IQR 23-259.5) 42.4% of 794 medical admissions were HIV infected. Over a quarter of HIV-related admissions were newly diagnosed on admission. 46.1% of patients on treatment were failing ART. More than 10% of HIV-infected patients had interrupted treatment with a similar number of patients previously known to be HIV infected having not yet initiated treatment. AIDS defining conditions accounted for more than 40% of reasons for admission.

Conclusion

Median CD4 counts remain low in hospitalised HIV positive patients despite universal access to ART. Large numbers of HIV patients are not accessing or are disengaging from HIV care.

Introduction

South Africa has the largest HIV epidemic in the world and therefore carries a large part of the global burden of the HIV/AIDS pandemic, with 19% of the worldwide population of people living with HIV infection, 15% of new infections and 11% of AIDS related deaths (1). South Africa has the largest antiretroviral treatment (ART) programme in the world, accounting for a fifth of people on antiretroviral therapy worldwide (1). In the country it is estimated that there are 7.7 million adults living with HIV with 7 million people knowing their status. There are 4.8 million people on ART (62% of people with HIV [95%CI: 57% - 66%]. 54% (95% CI: 49%-58%) of people with HIV have suppressed HIV viral loads. More than half (56%) of HIV patients are diagnosed late, with a CD4 count <350 cells/µl (1).

Since 2004 there has been a substantial increase in access to ART in South Africa with numerous changes to National HIV Treatment Guidelines and expansions in ART eligibility from an initial threshold for ART eligibility of a CD4 count < 200 cells/µl at the start of the treatment rollout in 2004, to currently providing treatment to all people living with HIV infection who present for care as of September 2016 with a universal test and treat policy (2, 3).

The proportion of patients newly diagnosed with advanced HIV is decreasing showing some success of the universal test and treat policy (4). However 15 years since ART rollout, challenges remain. South Africa is still suffering from numerous

areas of breakdown in the HIV “cascade of care” resulting in complications and death from HIV related illnesses (5), and hospitals are still admitting a large number of patients with HIV-related conditions (6). From June 2012 to October 2013, almost a decade into the ART era in the country, over 60% of all medical admissions in a district hospital in Cape Town were HIV-related (7). Up to 15% of the HIV-infected patients, at the same hospital, were newly diagnosed on admission and nearly a quarter of those known to be HIV infected prior to admission were ART naïve. Among hospitalized patients on ART nearly 50% were not virologically suppressed (7). A study conducted in Johannesburg, at a regional public-sector hospital found that nearly half of the medical admissions were HIV infected with mortality rates being higher amongst the HIV infected patients compared to HIV non-infected (6).

The HIV epidemic in South Africa has now matured with increased access to ART and a strategy of universal “Test and Treat”. As such, it is an appropriate time to review data predating universal test and treat, and compare to data from the current treatment policy. With low CD4 counts, despite increased access to treatment, patients will be predisposed to opportunistic infections and the complications of HIV, thus highlighting the extreme burden South African Hospitals still face. This makes it vital to identify inpatient epidemiological, clinical and laboratory characteristics, during the current policy of treating HIV regardless of CD4 counts, in order to develop strategies to achieve the UNAIDS goals known as “90 90 90” in hospitalized patients(8).

Therefore the aim of this study was to assess the proportion of patients being admitted to general medical wards at a tertiary hospital that are HIV infected and to determine the median CD4 count for these patients in order to add information on

the current state of the HIV pandemic, almost 15 years into the ART era. Additionally we sought to describe the demographics of HIV admissions (mean age, employment status and gender) of HIV infected patients being admitted and to determine the reasons for hospital admissions among HIV infected patients.

Methods

The study was a prospective, descriptive study of general medical patient admissions to a single medical unit. Ethics approval was obtained from the CEO office and research committee at Helen Joseph Hospital as well as the University of Witwatersrand Human Research Ethics Committee (Medical) for the research to be conducted (Appendix 3.5).

Site and Population

Research was conducted at Helen Joseph Hospital, in Johannesburg South Africa, a public-sector tertiary institution forming part of the University of the Witwatersrand's Department of Internal Medicine which provides tertiary level healthcare to a regional population of approximately 1 million people. The hospital has 21 in-patient wards, including 11 medical wards. There are 4 medical units each taking in new admissions on intake every 4 days. On average there are 30 to 40 new medical admissions per day.

The study population was all medical patients admitted by a single medical unit during general medical intakes at Helen Joseph Hospital from September 2018 to January 2019.ART was freely available to all patients during this period.

Data collection

Data was collected from patients as they were admitted to the general medical wards. No personal identification details of patients were collected in this study. Patients gave informed consent prior to their results being accessed. We collected results of tests from patient's medical records and baseline admission data. We collected patient demographics, patients HIV status, ART status if HIV infected (as per definitions below), reasons for admission and virological status.

Definitions

Treatment naïve is defined as HIV infected patients who have never been on ART.

Currently on ART with previous interruption is classified as HIV infected patients taking ART on admission but having interrupted therapy for more than 5 days previously.

Treatment interrupted describes HIV infected patients not on ART for at least 5 days at admission but was previously on ART.

Virological failure was defined as per the World Health Organisation (WHO) definition: Plasma viral load above 1000 copies/ mL based on two consecutive viral load measurements after 3 months, with adherence support (9). However for the purpose of the study patients were deemed to be failing treatment if found to have a viral load above 1000 copies/mL on a single occasion as patients were only seen once in the study.

Tuberculosis infection (TB) was defined a positive Gene Xpert or Tb culture on sputum, cerebrospinal fluid, pleural fluid, fine needle aspiration, ascitic fluid or a positive urine LAM

Data Analysis

We described the population using descriptive statistics: we estimated the mean age of all admissions, and median CD4 counts and viral loads along with interquartile ranges (IQR) for all HIV infected admissions. We compared the risk of admission due to non-communicable diseases between HIV infected and negative patients.

Results

Data was collected from a total of 794 patients who were admitted to 1 of the 4 medical units at Helen Joseph Hospital during the course of the study from September 2018 to January 2019 (figure 1). 337 patients were HIV infected (42.4%, 95% CI: 39% to 46%) while 214 patients tested HIV non-infected and 243 patients were not tested on admission. Of the HIV infected patients, 246 (73%, 95% CI: 68% to 78% of HIV infected admissions) were previously known to be HIV infected prior to admission while 91 patients (27%, 95% CI: 22% to 32**%** of HIV admissions) were newly diagnosed HIV infected on admission (figure1).

Demographics

The demographic characteristics of the study population are summarised in Table 1. The mean age of all HIV infected admissions was 40.7 years, while that of the HIV non-infected was 49.7 and those not tested was 57.4 years. The mean age of newly diagnosed HIV infected patients was 39.8 years. Those on treatment had a higher mean age of 43.3, while that of patients who had interrupted treatment was 40. The ART naïve and patients who had interrupted had lower mean ages of 35.3 and 37.9 years respectively (Table 1). There was a slightly higher proportion of male HIV infected admissions compared to females. Male admissions accounted for 51% (n=

172) of all HIV infected patients and 59.3% (n=54) of newly diagnosed HIV infected patients. 52% of patients who had interrupted ART were male. The majority of admitted HIV infected patients were unemployed (58.4%) compared to only 36.3% of patients who tested HIV non-infected or were not tested. Nearly 80% of patients who had interrupted treatment were unemployed while over 60% of newly diagnosed HIV infected patients were unemployed (Table 1).

ART History

191 (77.6%) patients known to be HIV infected were on ART on admission. 48 of these patients (25% of all patients on ART) had previously interrupted treatment. Almost 12% of patients known to be HIV infected had interrupted treatment (i.e. stopped taking ART for at least 5 consecutive days). 10.5% of patients previously known to be HIV infected had not yet initiated treatment despite already knowing their HIV infected status (ARV naïve).

CD4 count and viral load

Among those newly diagnosed with HIV, 10 patients were not tested for CD4 cell counts and 28 did not have a viral load test. In the previously known HIV infected group 17 were not tested for CD4 count and 36 did not have a viral load test.

Among all HIV infected patients, median CD4 cell count was 67 cells/µl (IQR 23-259.5) and median viral load was 31,400 copies/ml (IQR 96.5 - 421,000). Amongst newly diagnosed HIV infected admissions, median CD4 count was 44 cells/µl (IQR 13-108) and median viral load was 438 000 copies/ml (IQR 180,250- 1,255,000). Patients who had interrupted ART had a median CD4 count of 92 cells/µl (IQR 16-

147.5) and median viral load of 957.5 copies/ml (IQR 13,350 – 404,500) (see table 2).

Virological failure accounted for 26.1% of all HIV infected admissions, just under half of all patients on ART with 32.9% of patients on treatment without interruption and 85% of patients who had previously interrupted treatment.

Reasons for admission and comorbid Illnesses

The most frequent reason for admission among HIV infected patients (table 4) was tuberculosis (TB) (N=76, 22.6% of all HIV infected admissions). Five patients (6.6% of all patients admitted with TB) had multidrug resistant TB. 59 patients were admitted with AIDS defining illnesses (17.5% of all HIV infected admissions) being admitted. These included: *Pneumocystis Jirovecci* Pneumonia (n=22), cryptococcal meningitis (n=11), Cryptosporidium infection (n=2), disseminated Herpes Simplex infection (n=2), and disseminated Cytomegalovirus infection (n=1), Mycobacterium Avium Complex infections (n=2) and AIDS defining malignancies (n=8). Bacterial infections were the next most common reason for admission with 17.2% of all HIV infected admissions (N= 58), including bacterial pneumonia, bacterial meningitis and urinary tract infections

Non-communicable diseases (Hypertension, Diabetes Mellitus, Chronic Obstructive Pulmonary Disease, and heart disease) accounted for 19 admissions (Table 4) among HIV infected patients (5.6%) compared to 149 patients who were HIV non-infected or not tested (Table 5) being admitted for non-communicable disease (NCDs) (32.6%). The relative risk of being admitted due to a NCD when comparing HIV infected to negative/ not tested patients was 0.2 (95% CI: 0.1 to 0.3).

Other reasons for admission in HIV infected patients (Table 4) included central nervous system (CNS) disorders (26 patients) including stroke, seizures, peripheral neuropathy and other CNS infections, drug related conditions (10 patients) such as hypersensitivity side effects, drug related liver injury and Efavirenz neurological toxicity.

27 HIV infected patients (8% of all HIV infected admissions) had comorbid NCDs. In contrast, 58 HIV non-infected and 63 patients that were not tested for HIV (total of 214 patients; 27% of all HIV non-infected and 26% of HIV unknown patients) were admitted with these co morbidities. We found a relative risk of 0.2 (95% confidence interval: 0.1-0.2); comparing the ratio of HIV infected to HIV non-infected/not tested patients having comorbid NCDs.

Interruption of ART

A quarter of patients on ART had previously interrupted treatment. The most frequent reason for treatment interruption was “no reason” while the next most common reason was forgetting to take treatment, patients denying their status despite a documented HIV infected status, and patients lacking insight into their condition to take daily treatment (Table 3). Insight was assessed by the examiner upon questioning the patient. Social reasons, including travelling, unable to afford travel to clinic, food insecurity, child reliant on a caregiver and social influence accounted for 29.9% of reasons for interrupting. Drug-related side effects and social stigma each accounted for 8 patients (10.3 %).

Discussion

This study depicts how the proportion of HIV patients being admitted remains high even with the increased access to ART. 42.4% of all medical patients were found to be HIV infected on admission, over a quarter (27%) of these patients were newly diagnosed on admission and still, in this era of universal access to ART, almost half of the patients on ART were virologically failing at the time of admission.

For all HIV infected patients, median CD4 cell count was 67 cells/µl (IQR 23-259.5) and median viral load was 31,400 copies/ml (IQR 96.5-421 000). Newly diagnosed patients had a lower median CD4 count as would be expected of 44 cells/µl . Even patients on treatment had low median CD4 counts of 100 cells/µl. This illustrates how median CD4 counts, among hospitalised patients, have remained low when compared to earlier studies before the policy of universal test and treat, even within the same hospital and city(6,7,10,11,12). This depicts how HIV infected inpatients are still predisposed to AIDS defining conditions due to their low CD4 cell counts.

In terms of reasons for admission, over 40% of HIV patients were admitted for TB and AIDS defining conditions. HIV infected patients were less likely than HIV non-infected/not tested patients to be admitted due to non-communicable diseases. The most frequent reason for admission among HIV infected admissions remains TB followed by other AIDS defining conditions and bacterial infections, as shown previously in a recent systematic review and meta-analysis (13), highlighting the persistence of these illnesses as a large burden on the health system despite increased ART access.

The reasons for persistently low median CD4 counts in hospitalized patients despite universal access to ART, remain unclear. However possible hypotheses are the significant social and financial constraints on the population within South Africa. The

majority of HIV infected patients admitted in this study were unemployed (58.4%) More than two thirds of patients who had interrupted treatment were unemployed while over 60% of newly diagnosed HIV infected patients were unemployed. This highlights a possible association of unemployment with poor ART outcomes and late presentation which would require further investigation.

This study may suggest that social reasons for interrupting treatment such as transport costs and work related travel are still playing a large role as suggested by earlier research (14, 15). Major social interventions would need to be implemented to address these issues. There is growing evidence that Differentiated Service Delivery may be a successful approach to tackle some of these issues. These interventions include adherence support clubs, conception and family planning, service delivery to specific high risk groups as well as more decentralised centres of care (5, 8, 16).

A quarter of patients on ART had previously interrupted their treatment and nearly 10% of all HIV infected admissions had interrupted treatment completely at admission. There was no difference in median viral load and little difference in median CD4 cell count between these groups.

The most common reason for treatment interruption in this study was “no reason”. This was the response given by patients in their own words when asked about why they had interrupted treatment. This indicates a concerning disengagement from care as patients were not even willing to engage with a healthcare worker as to the reason for their treatment interruption. Possible reasons for this could be stigma round HIV diagnosis, distrust of healthcare workers, language barriers, denial and unwillingness to disclose social and monetary barriers to accessing care. 10.5% of all HIV admissions in the study already had a positive status on admission but had

not yet initiated treatment, again showing an alarming failure of linkage to care. This is in keeping with a trend that there are still an appreciable number of patients who should have been started on ART but have not yet done so (4). This again may be due to a number of factors including patient factors such as stigma, costs of travel to and from clinics and heath care provider factors such as stock outs, long waiting times, staff shortage and inadequate communication between health professionals and patients (14). This together with the high treatment interruption rate and large numbers of patients with unsuppressed viral loads shows that the successes made in treating regardless of CD4 count are being countered by a significant population of patients that represent due to interrupting treatment, poor adherence and virological failure (4).

Within developed countries, there is a growing aging population of HIV infected patients and the proportion of HIV infected patients diagnosed with NCDs is rising (17, 18). However even with increased access to ART in South Africa, our study showed 19 patients of 337 HIV infected admissions were admitted for NCDs (Table 4 and Figure 2) with over 40% of HIV patients being admitted for AIDS defining conditions. The mean age of all HIV patients was 40.7 years .The median CD4 cell count of HIV infected patients in this study who presented with NCDs was 123 cells/µl (IQR 33-352.5), while that of patients presenting due to HIV associated complications had a lower median CD4 count 100 cells/µl (IQR 28-350). This illustrates how hospitals in South Africa are still struggling to prevent HIV related complications due to low CD4 counts even in patients on ART and seeing care for NCDs.

Sex differences in HIV prevalence is most prominent among young adults being three times higher among females than males, especially amongst young adults (19, 20, 21). A recent study showed that patients initiating ART in South Africa are predominantly female (21) and in the Themba Lethu study 61% of patients initiating ART were female (10). In contrast our study showed 51% of all HIV infected admissions were male. Nearly 60% of patients newly diagnosed were male and 52% of patients having interrupted treatment were male. This may be in keeping with the earlier South African study (21) which showed men were more likely to start ART at lower CD4 counts, and men having poorer access to HIV services (15, 20, 21, 22) thus possibly accounting for their high rates of being newly diagnosed on admission.

A worryingly large number of patients were not tested for HIV on admission to hospital (figure 1). Reasons for this may be patients' unwillingness to consent to testing, patients unable to consent due to medical illness and patients possibly were not tested on admission but later during their hospital stay.

Within South Africa, before the rollout of ART, up to half of medical admissions to state hospitals were HIV related (6, 23). Years later into a sustained and comprehensive treatment plan, South African hospitals are still experiencing a high burden of HIV related illness (6).

Before the policy of test and treat regardless of CD4 count and universal access to ART, up to 60% of medical admissions were due to HIV related illnesses, up to 50% of patients on ART were not virally suppressed, high numbers of patients known to be HIV infected were still ARV naive and large numbers of patients were newly diagnosed on admission (6, 7). Some areas in the country are showing success in moving towards the UNAIDS 90 90m 90 targets (19, 24). However the situation

remains largely unchanged now within this new era of universal test and treat test within a hospital setting as shown by this study.

Limitations of this study are that it is a single centre study conducted over a short time span. Data was collected from September to January and so there may be seasonal variation in reasons for admission. Reasons for admission were based on initial assessment and not a discharge diagnosis. Confounding factors such as other causes for a decreased CD4 cell count were not addressed in this study. High numbers of patients were not tested for HIV and therefore some data may be missing and true numbers may not be accurate. The study population was patients from a secondary to tertiary level hospital and so may not be entirely representative of the larger population of HIV infected patients seeking outpatient treatment care. However it is representative of other urban inpatient cohorts in the country.

In conclusion the proportion of medical patients, who are HIV infected, being admitted to hospitals in South Africa remains largely unchanged in the era of ART regardless of CD4 cell counts. Reasons for admission among HIV infected patients have remained the same. There has also been little change in the median CD4 counts of patients admitted to Hospitals since before the universal test and treat era and similar rates of virological failure remain.

Table 1: Demographic characteristics of HIV non-infected, Unknown and HIV infected patients admitted during the study.

	HIV non-infected	HIV unknown/ not tested	All HIV infected	Newly Diagnosed HIV infected	On treatment (HIV infected)	Currently on ART with previous interruption (HIV infected)	ART naïve (HIV infected)	Interrupted ART (HIV infected not on Treatment)
Total patients	214	243	337	91	143	48	26	29
Mean age in years	49.7	57.4	40.7	39.8	43.3	40	35.3	37.9
Female	N=105(49.1%)	N=139(57.2%)	N=165 (49%)	N=37 (40.7%)	N=82 (57.3%)	N=21(43.8%)	N=11 (42.3%)	N=14 (48%)
Male	N=109 (50.9%)	N=104(42.8%)	N=172 (51%)	N=54 (59.3%)	N=61 (43.7%)	N=27 (56.2%)	N=15 (57.7%)	N=15 (52%)
% of Total unemployed	43%	30.5%	58.4%	61.5%	49.7%	50%	69.2%	79.3%

Table 2: Laboratory characteristics of HIV infected patients admitted during study.

		All HIV infected	Newly Diagnosed HIV infected	On Treatment without interruption	Currently on ART with previous interruption	ARV naïve (known HIV positive not on ART)	Interrupted ART
CD4 cell count (cells/µl)	Median	67	44	100	100	100	92
	IQR	23-259.5	13-108	30.2- 350.6	28--350	31- 354.5	28- 351
Viral Load (copies/ml	Median	31 400	438 000	862	957.5	778	957.5
	IQR	96.5-421000	180 250-1 255 000	20- 123 000	20- 133250	20-105750	20.8-139750

Table 3: Reasons given for interrupting ART among HIV infected patients admitted to hospital.

Reasons for Interrupting	Number of patients
No Reason	18
Forgets/denial/Lack of insight into treatment	13
unable to afford transport to clinic	10
Travel related/ travelling for work	9
Drug Side Effects	8
Social Stigma	8
Depression/ Psychosis	5
Food insecurity	2
child dependent on parent to get tabs	1
traditional healer advising to stop	1
Clinic Pill Shortage	1

Table 4: Reasons for admission amongst HIV infected patients.

	Newly Diagnosed HIV infected (number of patients)	Previously Known HIV infected (number of patients)	Not on ART/ Interrupted ART (number of patients)
TB	26	33	17
Bacterial Infections	15	32	11
HIV Associated Infections	17	21	15
AIDS Defining Malignancies	1	5	0
Drug Related Conditions (side effects/toxicity)	1	9	0
NON communicable Disease	4	14	1
Gastroenteritis	2	20	5
Renal Dysfunction	2	1	3
Liver Dysfunction/ Hepatitis B	1	3	1
CNS Disorders	9	16	1
Venous Thromboembolic Disease	1	4	0
Anaemia	2	9	1
Psychiatric Illness	1	3	3

Table 5: Showing Reasons for Admission for HIV non-infected /not tested Patients

Reason for admission	HIV non-infected (number of patients)	HIV unknown (number of patients)
TB	4	0
Bacterial Infections	31	29
Drug Related Conditions (side effects/ toxicity)	1	6
Non Communicable Diseases	63	58
Gastroenteritis	8	4
Renal Dysfunction	12	4
Liver Dysfunction	11	4
CNS Disorders	22	17
Venous Thromboembolic Disease	6	7
Anaemia	5	10
Psychiatric Illness	11	21

Figure 1: Flow diagram showing the total number of patients admitted during the study, numbers of HIV infected and negative, ART status of HIV infected patients.

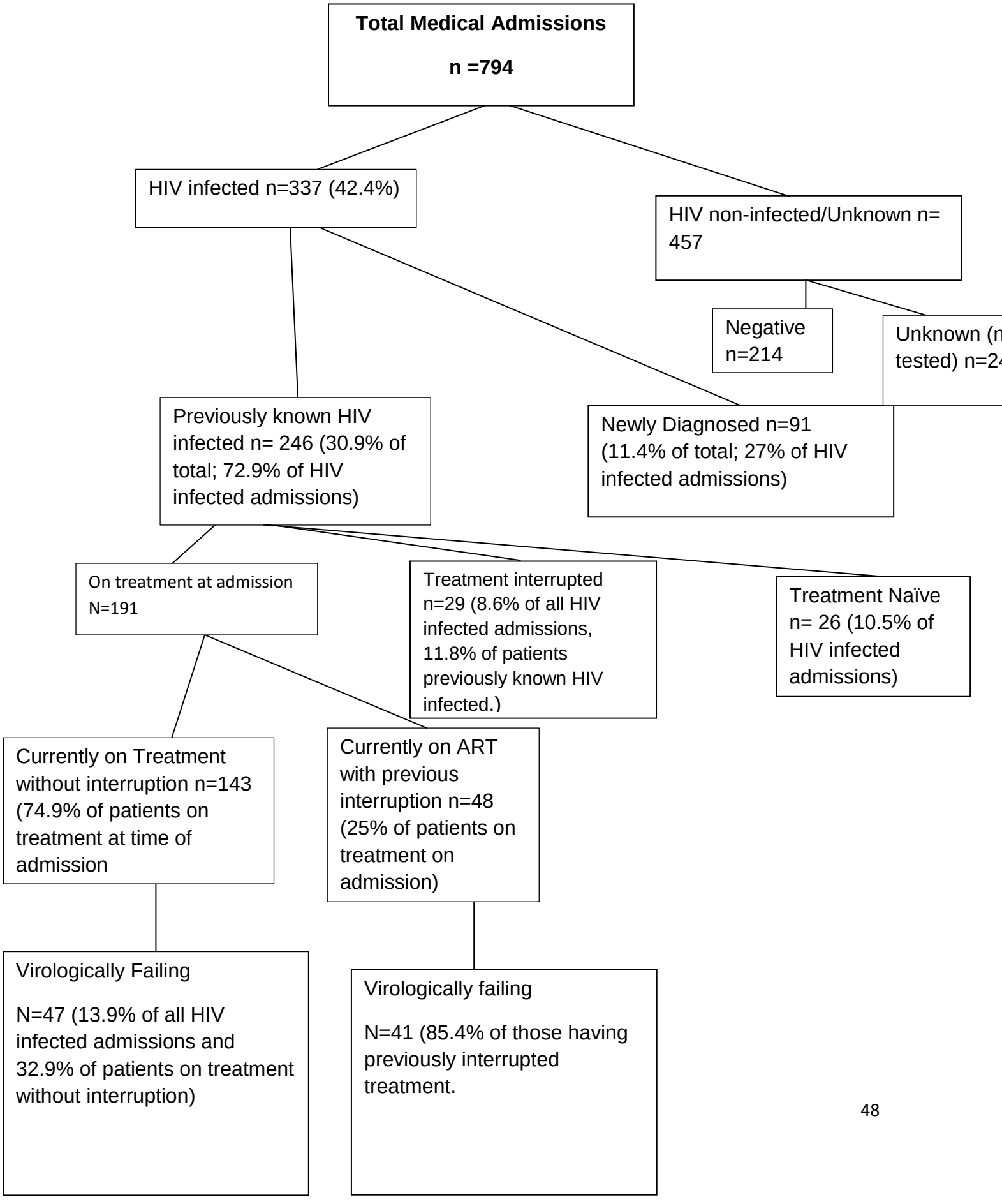
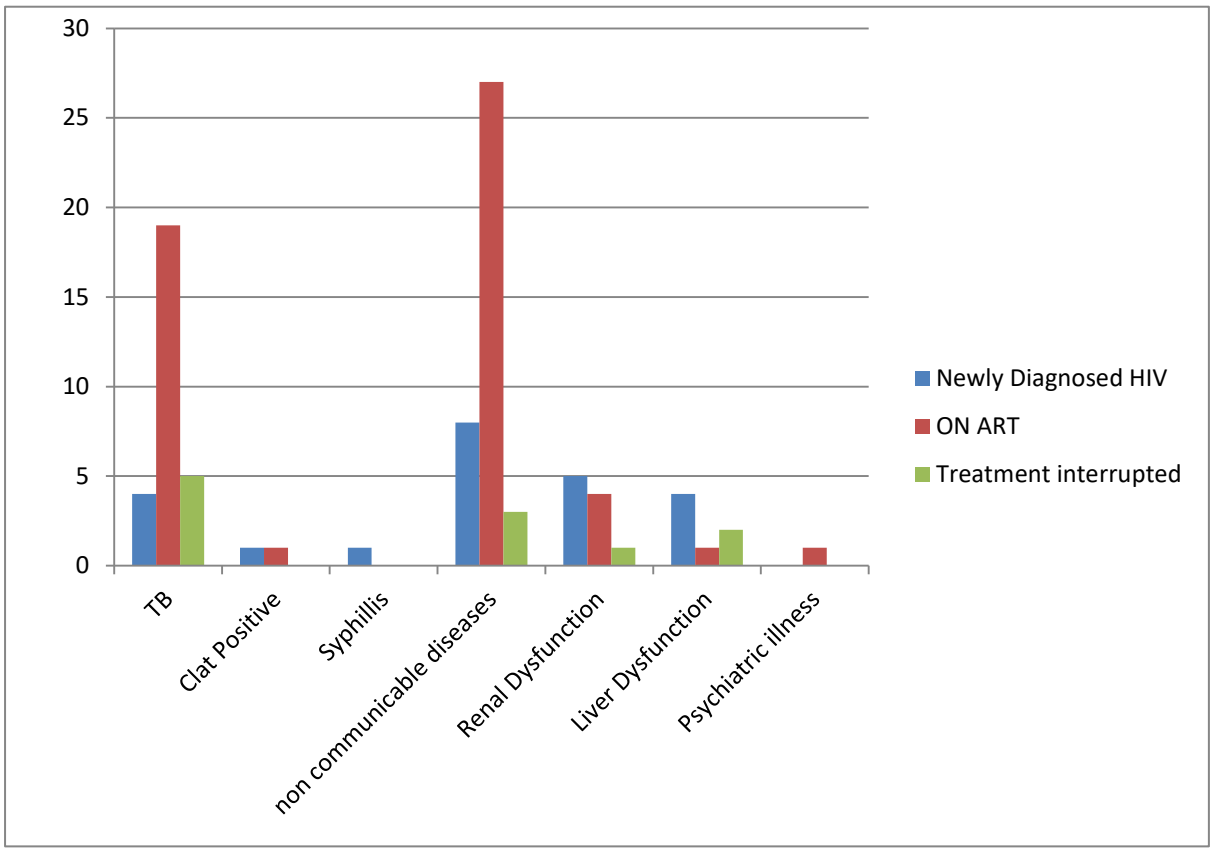


Figure 2: Co morbid Illnesses among HIV infected Admissions



References

1. South Africa | UNAIDS [Internet]. [Cited 2018 Mar 14]. Available from: http://www.unaids.org/en/regionscountries/countries/southafrica

2. Katz IT, Kaplan R, Fitzmaurice G, Leone D, Bangsberg DR, Bekker L-G, Orrell C. Treatment guidelines and early loss from care for people living with HIV in Cape Town, South Africa: A retrospective cohort study. Deeks SG, editor. PLoS Med [Internet]. 2017 Nov 14 [cited 2018 Mar 14]; 14(11):e1002434. Available from: http://dx.plos.org/10.1371/journal.pmed.1002434

3. Meintjes G, Moorhouse MA, Carmona S, N Davies, S Dlamini, C Van Vuuren, T Manzini, M Mathe, Y Moosa J Nash, J Nel, Y Pakade, J Woods, G Van Zyl, F Conradie, F Venter. Adult antiretroviral therapy guidelines 2017. S Afr J HIV Med. 2017; 18(1), a776. https://doi.org/10.4102/ sajhivmed.v18i1.776

4. Osler M, Hilderbrand K, Goemaere E, Ford N, Smith M, Meintjes G, Kruger J, Govender N, Boulle A. The Continuing Burden of Advanced HIV Disease Over 10 Years of Increasing Antiretroviral Therapy Coverage in South Africa. Clin Infect Dis [Internet]. 2018 Mar 4 [cited 2019 Apr 12]; 66(suppl_2):S118–25. Available from: http://www.ncbi.nlm.nih.gov/pubmed/29514233

5. Venter F, Ford N, Vitoria M, Stevens W. Diagnosis and monitoring of HIV programmes to support treatment initiation and follow up and improve programme quality. Curr Opin HIV AIDS [Internet]. 2017 Mar [cited 2019 Jun 11];12(2):117–22. Available from: http://www.ncbi.nlm.nih.gov/pubmed/28134712

6. Long LC, Fox MP, Sauls C, Evans D, Sanne I, Rosen SB. The High Cost of HIV-Positive Inpatient Care at an Urban Hospital in Johannesburg, South Africa. Fischer G, editor. PLoS One [Internet]. 2016 Feb 17 [cited 2018 Mar 14]; 11(2):e0148546. Available from: http://dx.plos.org/10.1371/journal.pone.0148546

7. Meintjes G, Kerkhoff AD, Burton R, Schutz C, Boulle A, Van Wyk G, Blumenthal L, Nicol M, Lawn S. HIV-Related Medical Admissions to a South African District Hospital Remain Frequent Despite Effective Antiretroviral Therapy Scale-Up. Medicine (Baltimore) [Internet]. 2015 Dec [cited 2018 Mar 14]; 94(50):e2269. Available from: https://insights.ovid.com/crossref?an=00005792-201512150-00045

8. Darling KE, Hachfeld A, Cavassini M, Kirk O, Furrer H, Wandeler G. Late presentation to HIV care despite good access to health services: current epidemiological trends and how to do better. Swiss Med Wkly [Internet]. 2016 Aug 21 [cited 2018 Mar 14]; 146:w14348. Available from: http://doi.emh.ch/smw.2016.14348

9. Who.int. 2018 [cited 30 January 2018]. Available from: http://www.who.int/hiv/pub/guidelines/arv2013/art/WHO_CG_table_7.15.pdf

10. Budgell EP, Maskew M, Long L, Sanne I, Fox MP. Brief Report: Does Most Mortality in Patients on ART Occur in Care or After Lost to Follow-Up? Evidence From the Themba Lethu Clinic, South Africa. J Acquir Immune Defic Syndr [Internet]. 2015 Nov 1 [cited 2019 Apr 12]; 70(3):323–8. Available from: http://www.ncbi.nlm.nih.gov/pubmed/26181816

11. Pandie M, Van der Plas H, Maartens G, Mendelson M. The role of the infectious diseases unit at Groote Schuur Hospital in addressing South Africa's greatest burden of disease. S Afr Med J [Internet]. 2012 May 23 [cited 2018 Mar 14]; 102(6):528–31. Available from: http://www.ncbi.nlm.nih.gov/pubmed/22668956

12. Mkoko P, Raine RI. HIV-positive patients in the intensive care unit: A retrospective audit. S Afr Med J [Internet]. 2017 Sep 22 [cited 2018 Mar 14]; 107(10):877–81. Available from: http://www.ncbi.nlm.nih.gov/pubmed/29022532

13. Ford N, Shubber Z, Meintjes G, Grinsztejn B, Eholie S, Mills EJ, Davies MA, Vitoria M, Penazzato M, Nsanzimana S, Frigati L, O'Brien D, Ellman T, Ajose O, Calmy A, Doherty M. Causes of hospital admission among people living with HIV worldwide: a systematic review and meta-analysis. Lancet HIV [Internet]. 2015 Oct [cited 2018 Mar 14]; 2(10):e438–44. Available from: http://www.ncbi.nlm.nih.gov/pubmed/26423651 /

14. Bor J, Chiu C, Ahmed S, Katz I, Fox MP, Rosen S, Yapa M, Tanser F, Pillay D, Bärnighausen T. Failure to initiate HIV treatment in patients with high CD4 counts: evidence from demographic surveillance in rural South Africa. Trop Med Int Health [Internet]. 2018 [cited 2019 Apr 12]; 23(2):206. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5829292

15. Johnson LF, Rehle TM, Jooste S, Bekker L-G. Rates of HIV testing and diagnosis in South Africa: successes and challenges. AIDS [Internet]. 2015 Jul 17 [cited 2019 Apr 16]; 29(11):1401–9. Available from: http://www.ncbi.nlm.nih.gov/pubmed/26091299

16. Ehrenkranz P, Grimsrud A, Rabkin M. Differentiated service delivery: navigating the path to scale. Curr Opin HIV AIDS [Internet]. 2019 Jan [cited 2019 Jul 30];14(1):60–5. Available from: http://www.ncbi.nlm.nih.gov/pubmed/30394947

17. Smit M, Cassidy R, Cozzi-Lepri A, Quiros-Roldan E, Girardi E, Mammone A, Antinori A, Saracino A, Bai F, Rusconi S, Magnani G, Castelli F, Hsue P, d'Arminio Monforte A, Hallett TB. Projections of non-communicable disease and health care costs among HIV-positive persons in Italy and the U.S.A.: A modelling study. Ceccherini-Silberstein F, editor. PLoS One [Internet]. 2017 Oct 23 [cited 2019 Sep 9];12(10):e0186638. Available from: http://www.ncbi.nlm.nih.gov/pubmed/29059202

18. Smit M, Brinkman K, Geerlings S, Smit C, Thyagarajan K, Sighem A van, de Wolf F, Hallett T; ATHENA observational cohort. Future challenges for clinical care of an ageing population infected with HIV: a modelling study. Lancet Infect Dis [Internet]. 2015 Jul [cited 2019 Sep 9];15(7):810–8. Available from: https://linkinghub.elsevier.com/retrieve/pii/S1473309915000560

19. HIV Impact Assessment Summary [Internet]. 2018 [cited 2019 Apr 15]. Available from: http://www.hsrc.ac.za/uploads/pageContent/9234/SABSSMV_Impact_Assess

20. Cornell M, Schomaker M, Garone DB, Giddy J, Hoffmann CJ, Lessells R, Maskew M, Prozesky H, Wood R, Johnson L, Egger M, Boulle A, Myer L. Gender Differences in Survival among Adult Patients Starting Antiretroviral Therapy in South Africa: A Multicentre Cohort Study. Celentano DD, editor. PLoS Med [Internet]. 2012 Sep 4 [cited 2019 Apr 16]; 9(9):e1001304. Available from: https://dx.plos.org/10.1371/journal.pmed.1001304

21. Cornell M, Johnson LF, Wood R, Tanser F, Fox MP, Prozesky H, Schomaker M, Egger M, Davies MA, Boulle A . Twelve-year mortality in adults initiating antiretroviral therapy in South Africa. J Int AIDS Soc [Internet]. 2017 [cited 2019 Apr 12]; 20(1):21902. Available from: http://www.ncbi.nlm.nih.gov/pubmed/28953328

22. Muula AS, Ngulube TJ, Siziya S, Makupe CM, Umar E, Prozesky HW, Wiysonge C, Mataya R. Gender distribution of adult patients on highly active antiretroviral therapy (HAART) in Southern Africa: a systematic review. BMC Public Health [Internet]. 2007 Apr 25 [cited 2019 Apr 16]; 7:63. Available from: http://www.ncbi.nlm.nih.gov/pubmed/17459154

23. Colvin M, Dawood S, Kleinschmidt I, Mullick S, Lallo U. Prevalence of HIV and HIV-related diseases in the adult medical wards of a tertiary hospital in Durban, South Africa. Int J STD AIDS [Internet]. 2001 Jun 25 [cited 2018 Mar 14]; 12(6):386–9. Available from: http://journals.sagepub.com/doi/10.1258/0956462011923336

24. Euvrard J, Schulz T, Hilderbrand K, Bosland M, Osler M, Boulle A, Davies M-A. How accurately do routinely reported HIV viral load suppression proportions reflect progress towards the 90-90-90 target in the population on antiretroviral treatment in Khayelitsha, South Africa? South African Med J [Internet]. 2019 Feb 26 [cited 2019 Jul 1];109(3):174. Available from: http://www.samj.org.za/index.php/samj/article/view/12564

3. Appendices

3.1 Data collection table

Age	
Gender	
Occupation	
HIV infected/ Negative	
Previously Known HIV infected	
CD4 Count	
Viral Load	
Newly Diagnosed HIV infected on admission	
On ART currently	
Interrupted Treatment	
Reason for interrupting	
Reason for admission	
Co-morbid Illness	

3.2 Patient Information Sheet

STUDY INFORMATION PAGE

An Audit of HIV infected Patients Admitted to Helen Joseph Hospital in Johannesburg, South Africa

Dear potential study participant

Please read the information below explaining the research that I am conducting. Any questions you have will be welcomed.

I am inviting you to take part in this research study

Aim of Study:

- To describe the epidemiology of HIV infection in a Tertiary Hospital setting
- To determine the reasons for hospital admissions among HIV infected patients
- to estimate the proportion of medical patients being admitted to general medical wards that are HIV infected
- to calculate the median CD4 count for these patients to be used as a marker of the current situation of the HIV pandemic

Study Participants

All medical patients admitted by a single medical unit during general medical intakes at Helen Joseph Hospital from November 2018 to March 2019

How the study will be conducted:

Data will be collected from patients as they are admitted to the general medical wards. No personal identification details of patients will be revealed in this study. Patients will remain anonymous. Results of tests from patient's medical records will be used. These tests will only be done if required as part of routine standard of patient care (or previously done) and no additional and unnecessary tests will be conducted and no additional costs will be incurred by the hospital or patient. Data will

be collected from Helen Joseph Hospital from November 2018 to March 2019. Only medical records of patients will be used. If found to be HIV infected, the results will be used but no names or identifiable numbers will be recorded. CD4 counts will be tested and recorded only if required during their inpatient care.

Data to be collected from Research participant:

- Gender
- Age
- Occupation
- If ARV naïve/ on Treatment/ interrupted ART
- Reasons for interrupting ART
- CD4 count
- Viral load
- Reasons for admission and other diseases

Potential Risks of being involved:

No blood samples will be collected specifically for this study, only biomedical and clinical data from tests conducted as part of routine care will be extracted from existing records that are routinely collected at the study sites as part of routine patient care. The study therefore poses no physical risks to patients. A possible risk is loss of confidentiality. Data being collected will indicate individuals' HIV status. This risk will be protected against by the fact that no patients' identifiers will be collected and a master list of data will be stored in a password protected document. Data will be captured on site and therefore no written records containing identifiers will leave the study sites. All personal information will be treated in the strictest confidence, as mentioned above it will not be recorded, and will only be available to the Principal Investigator (PI) and his Supervisor. The only exceptions would be:

1. personal information may be disclosed if required by law
2. the Human Research Ethics Committees of the University may exceptionally require personal data to respond to a formal complaint, or for a compliance audit
3. the South African Health Products Regulatory Authority (SAHPRA), which is the successor body to the South African Medicines Control Council (SAMCC), might conceivably require access to personal data, if conducting an investigation into a drug trial

Benefits of being in the study:

There is no direct benefit to the participant. However if the objectives of the study are met it may help benefit future patients and may provide information to help curb the HIV pandemic

Please note that Participation is voluntary. Refusal to participate will involve no penalty and patients will not be discriminated against in any form and will still receive the same satisfactory medical care as those who do participate. Participants may discontinue participation at any time without penalty, or loss of benefits to which the

Participant is otherwise entitled. There is no requirement to provide a reason for withdrawing and any data collected on such a person will be destroyed, unless the Participant specifically consents to its retention.

Contact details of researcher/s:
Dr Gregory Yudelowitz
Principal Investigator, telephone no. 0836846493, or by e-mail at gregyudels@gmail.com

Prudence Ive, Supervisor, by e-mail at pure.ive@gmail.com

This study has been approved by the Human Research Ethics Committee (Medical) of the University of the Witwatersrand, Johannesburg ("Committee"). A principal function of this Committee is to safeguard the rights and dignity of all human subjects who agree to participate in a research project and the integrity of the research.
If you have any concern over the way the study is being conducted, please contact the Chairperson of this Committee who is Professor Clement Penny, who may be contacted on telephone number 011 717 2301, or by e-mail on Clement.Penny@wits.ac.za. The telephone numbers for the Committee secretariat are 011 717 2700/1234 and the e-mail addresses are Zanele.Ndlovu@wits.ac.za and Rhulani.Mukansi@wits.ac.za

Thank you for reading this Study Information Sheet.

November 2018

3.3 Informed consent Form

PARTICIPANT CONSENT SHEET

An Audit of HIV infected Patients Admitted to Helen Joseph Hospital in Johannesburg, South Africa

1. I have been given a Participant Information Sheet which explains the nature and processes involved in this study, which is attached
2. I was given time to read it, or had it read to me, in the language I best understand;
3. I have been given time to ask any questions I wanted to and found any answers given to me to be reasonable and satisfactory;
4. I believe I fully understand why the study is being conducted and what the intended outcomes will be
5. I understand that there will be no immediate benefit to me, should I agree to participate, nor will I receive any payment; conversely, participation will not cost me anything but my time
6. I understand that, even if I initially consent to take part in the study, I may subsequently withdraw at any time and would not be required to give any reasons; if that happened, any data collected about me for the purposes of the study would immediately be destroyed, unless I give consent for it to be retained
7. I have been given a range of contact details, listed below. If I require further information or become concerned about any aspect of this study I am free to speak to any of these contacts
8. I understand that my personal details will not be used in the study and only results from my medical records will be used.
9. I understand that if I refuse to participate I will not be discriminated against in any form and will still receive the same satisfactory medical care as if I do participate

Contact details:

Dr Gregory Yudelowitz

Principal Investigator, telephone no. 0836846493, or by e-mail at gregyudels@gmail.com

Prudence Ive, Supervisor, by e-mail at pure.ive@gmail.com

Professor CB Penny, Chairperson of the Human Research Ethics Committee (Medical) at the University of Witwatersrand, on telephone no. 011 717 2301, or by e-mail at Clement.Penny@wits.ac.za. Ms. Z Ndlovu or Mr Rhulani Mkansi, Committee Secretariat, telephone nos.: 011 717 2700 or 1234, or by e-mail at: Zanele.Ndlovu@wits.ac.za or Rhulani.Mkansi@wits.ac.za

Name of Participant: _____
Date: _____
Place: _____
Signature or mark _____
Witnessed by:
Name of Witness: _____
Signature: _____
Date: _____

3.4 Turnitin Originality Report

Document Viewer

Turnitin Originality Report

Processed on: 06-Nov-2019 4:25 PM SAST
ID: 1208278483
Word Count: 7649
Submitted: 1

302891:turnitin_doc.docx By Gregory Yudelowitz

Similarity Index	Similarity by Source	
18%	Internet Sources:	9%
	Publications:	11%
	Student Papers:	13%

include quoted | include bibliography | excluding matches < 5 words | mode: quickview (classic) report | Change mode | print | download

1% match (Internet from 27-Feb-2018)
http://www.unaids.org

1% match (publications)
Lara Fairall, Max O Bachmann, Carl Lombard, Venessa Timmerman et al. "Task shifting of antiretroviral treatment from doctors to primary-care nurses in South Africa (STRETCH): a pragmatic, parallel, cluster-randomised trial", The Lancet, 2012

1% match (publications)
P Mkoko, R I Raine. "HIV-positive patients in the intensive care unit: A retrospective audit", South African Medical Journal, 2017

1% match (student papers from 10-Sep-2019)
Submitted to Charterhouse on 2019-09-10

1% match (Internet from 17-Jan-2019)
https://www.r4d.org/wp-content/uploads/HIV-Financing-Integration-in-South-Africa-Full-Report.pdf

1% match (student papers from 27-May-2019)
Submitted to Intercollege on 2019-05-27

1% match (student papers from 03-Feb-2017)
Submitted to Imperial College of Science, Technology and Medicine on 2017-02-03

3.5 Ethics Clearance Certificate

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG	HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

Office of the Deputy Vice-Chancellor (Research & Post Graduate Affairs)

TO: Dr GS Yudelowitz
School of Clinical Medicine
Department of Medicine
Division of Internal Medicine
Helen Joseph Hospital

E-mail: gregyudels@gmail.com

CC: Supervisor: Drs P Ive and M Fox <Prue.Ive@gmail.com>
and <HREC-Medical.ResearchOffice@wits.ac.za>

FROM: Iain Burns
Human Research Ethics Committee (Medical)
Tel: 011 717 1252

E-mail: Iain.Burns@wits.ac.za

DATE: 01/06/2018

REF: *R14/49*

PROTOCOL NO: **M180310** *(This is your ethics application study reference number. Please quote this reference number in all correspondence relating to this study)*

PROJECT TITLE: *An Audit of HIV Patients Admitted to Helen Joseph Hospital in Johannesburg, South Africa*

Please find attached the Clearance Certificate for the above project. I hope it goes well and that an article in a recognized publication comes out of it. This will reflect well on your professional standing and contribute to the Government funding of the University.

MSWorks2000/Iain0007/Clearscan.wps