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Barriers to smoking cessation amongst people living with human immunodeficiency virus (HIV) in South Africa

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BARRIERS TO SMOKING CESSATION AMONGST PEOPLE LIVING WITH HUMAN IMMUNODEFICIENCY VIRUS (HIV) IN SOUTH AFRICA

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A Research report

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15 April, 2022

DECLARATION

I, Angela Morongwe Matsepe, do hereby declare that this research report is my unaided, own work. It is being submitted for the degree of Master of Medicine, Internal Medicine at the University of the Witwatersrand, Johannesburg. It has not been submitted previously for any other degree or examination at any other institution or university.

……

……. day of ……...2021 in Johannesburg

DEDICATION

My mother Gladys, for the many years of unconditional love, support, encouragement and prayers.

To my late father Stephens, I will always make you proud.

For my beloved daughter Lethabo.

PRESENTATIONS ORIGINATING FROM THIS RESEARCH

None

ETHICAL CLEARANCE

Permission to conduct the study was obtained from Professor C. Menezes (Internal Medicine academic head, University of the Witwatersrand, Faculty of Health Sciences), Management and the Medical Advisory Committee (MAC) at Chris Hani Baragwanath Academic Hospital, and the Human Research Ethics Committee, University of Witwatersrand (Clearance No. M1911120). The research is registered with National Health Research Database (NHRD): GP 202112 022.

ABSTRACT

Background: Antiretroviral therapy (ART) coverage in South Africa has improved the quality of life of people living with the human immunodeficiency virus (PLWH). Smoking remains a major modifiable risk factor for non-HIV-related morbidity and mortality. The adverse effects of smoking continue to threaten the positive gains made by an effective ART programme. The prevalence of smoking is higher in PLWH than in their HIV-negative counterparts, yet, in sub-Saharan Africa, little is known about barriers to smoking cessation amongst PLWH. To address this gap in knowledge, we conducted a questionnaire study involving PLWH who attended an adult ART clinic in Johannesburg, South Africa.

Objective: To describe barriers to smoking cessation for people living with HIV who attended the Chris Hani Baragwanath Academic Hospital Adult HIV Clinic in Johannesburg, South Africa.

Methods: A voluntary, anonymous questionnaire was completed by 189 ARV (antiretroviral) clinic attendees; their demographic and smoking-related data was recorded. A Fagerström score was used to assess their level of nicotine dependence.

Results: The mean age of people who completed the questionnaire was 45.4 years (standard deviation 11.77); 85.19% of participants were male. Overall unemployment was 65.61% and 70.31% had no matric qualification. The median number of years smoked was 19 (IQR 10–28 years) and the current median daily consumption was 6 cigarettes per day (IQR 4–10 cigarettes per day). The median Fagerström nicotine dependence score measure was 4 (IQR 2–5), which indicates low to moderate nicotine dependence. Overall, there were 179 (94.71%) individuals who were willing to quit smoking; the majority 134 (70.90%) of the total study participants had previously attempted to quit smoking.

The majority of smokers (92.59%) were not familiar with smoking cessation pharmacotherapy. Of those who had previously attempted cessation, 69.40%) reported stress as a reason for failed previous attempts to quit smoking and 55.97% reported nicotine craving as another barrier to quitting. Overall, 36.51% of study participants reported concomitant alcohol use.

Conclusions: An alarming number of PLWH were not familiar with smoking cessation modalities. Stress and nicotine cravings are some of the self-reported barriers to quitting smoking and, furthermore, concomitant alcohol use was reported. A significant majority of study participants reported a willingness to quit smoking, and this offers an opportunity to co-

address smoking cessation during each ARV clinic follow-up visit, to educate attendees about the different modalities and to offer psychosocial support. In conclusion, smoking cessation measures that address the observed barriers are of great importance for the comprehensive management of HIV and AIDS in resource-limited countries, given the higher prevalence of smoking in PLWH, and the associated health risks.

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LIST OF ABBREVIATIONS AND ACRONYMS

AIDS	Acquired immune deficiency syndrome
ACC	American College of Cardiology
ART	Antiretroviral therapy
ARV	Antiretroviral
CHBAH	Chris Hani Baragwanath Academic Hospital
COVID-19	2019 novel coronavirus disease
CYP3A4	Cytochrome P450 3A6
HIV	Human immune deficiency syndrome
IQR	Interquartile range
NMR	Nicotine Metabolite Ratio
PLWH	People living with HIV
SD	Standard deviation

CHAPTER 1: PROTOCOL WITH EXTENDED LITERATURE REVIEW

1.1 BACKGROUND

Human immunodeficiency virus (HIV) is now in its fourth decade, and remains a global pandemic with alarming spread in resource-limited countries, like those in sub-Saharan Africa and South-East Asia[1]. According to the United Nations Programme on HIV/AIDS, approximately 36.9 million people worldwide were living with HIV or the acquired immune deficiency syndrome (AIDS) in 2017, and, in 2020, approximately 37.6 million people across the globe were living with HIV[2].

South Africa is a country with a high HIV infection rate, and an estimated overall prevalence of approximately 13.0% reported in the year 2020[3].The total number of people living with HIV (PLWH) in South Africa was estimated to be approximately 7.8 million in 2020[3]. Increasing the coverage of antiretroviral therapy (ART) in South Africa has improved the quality of life of PLWH and, hence, increased survival and longevity[4]. This is evidenced by an increasing prevalence of HIV associated with a declining number of new infections, as people who are infected now live longer and have near-normal life expectancies[5].

Smoking has been described as a major hurdle in the fight against HIV and AIDS[6]. Smokers who are HIV-infected and on ART lose more life-years to smoking-related complications and diseases than to HIV-related complications alone and, furthermore, more than twice as many life years are lost by PLWH who smoke, compared to the HIV-negative general population who smoke[7].

The prevalence of current tobacco use in HIV-positive smokers in developed countries is estimated at between 40% and 74%[8–10]. A study in Australia in 2014 reports a 42% prevalence of current tobacco use in PLWH[9]. This is two to threefold higher than in the general population, which was estimated at only 20% in the United States in 2011[8]. In the era of antiretrovirals (ARV), good clinical outcomes in the control of HIV continue to be threatened by the undesired complications of tobacco-related cardiovascular, pulmonary and neoplastic diseases. Case-control studies show that acute coronary syndrome is nearly twice as high in PLWH who smoke than in HIV-negative controls[11].

1.2 HIV AND SMOKING

PLWH are predisposed to lung malignancies which tend to occur at a younger age and after a shorter duration of exposure to smoking [9]. HIV infection has been reported to be an independent risk factor for lung cancer even after controlling for confounders such as smoking and age [9,10]. ART-adherent smokers were found to be 6 to 13 times more likely to die from lung cancer than from traditional AIDS-related causes whereas mortality in individuals with incomplete ART adherence was attributed to AIDS-related complications and not lung cancer[13]. This may be explained by the fact that ART-adherent individuals experience less AIDS-related complications and have increased survival whereas ART-non adherent individuals have a higher overall mortality due to immunological and virological failure.

Smoking plays an important causal role in non-HIV-related illnesses that lead to premature morbidity and mortality in PLWH[14] and, hence, smoking remains a critical, modifiable risk factor. In South Africa, a national downward trend in smoking levels has been reported in the general population since the introduction of control measures for smoking in public areas[15]. In 2010, the national tobacco smoking levels were recorded at 19.4% (upper CI 24.1), declining to 18.2% (upper CI 23.8) by 2015. [12,64]. Tobacco use remains high and is on the rise in PLWH, requiring scaled-up action to reduce the risk of tobacco-related diseases[4]. Although a downward trend in smoking amongst the general population has been reported, the rising & higher tobacco use in PLWH may be due to the multiple biopsychosocial challenges and stressors that these individuals endure.

Despite a call at the National Institutes of Health State-of-the-Science conference for research to evaluate tobacco control interventions for PLWH[16], only a few studies have been conducted to address this issue. In South Africa, data on the prevalence of smoking in PLWH is limited, and the prevalence is between 15% and 34%[4,17,18]. A Johannesburg-based study comprising of 207 HIV-infected patients attending an ART roll-out clinic found that 15% were current smokers, with the majority being males[18]. Other studies, conducted in the North West and Western Cape provinces, report prevalence of 34%[4] and 22%[17] respectively. Analysis of data on tobacco use by PLWH from 28 low and middle-income countries also report a higher prevalence of smoking amongst HIV-positive men than HIV-positive women[19].

Smoking cessation efforts have largely been aimed at the general population and it is unclear if these treatment strategies are suitable, effective or even applicable to cohorts with population-specific concerns and other clinical issues, such as PLWH[8]. Some of the

perceived smoking cessation barriers reported in South Africa amongst PLWH include economic stressors, such as unemployment and poverty, and social or interpersonal stressors, such as lack of social support due to having HIV[20]. Alcohol is, furthermore, used as a coping mechanism to deal with stressful situations and, hence, alcohol use frequently co-exists with smoking[20].

Despite a high prevalence of smoking amongst PLWH in South Africa, high-quality evidence on interventions for smoking cessation is not available[6]. A cross-sectional survey study performed in the North West province of South Africa reported a strong association between current smoking and the use of other harmful substances, such as marijuana[3]. The study comprised of 1210 adults with HIV infection, 137 (31%) of men reported ever using marijuana, and this was more prevalent among smokers than non-smokers (n = 115 (48%) and n = 22 (11%), respectively [3]. This practice may be a contributing barrier for successfully quitting smoking. There is a growing need to focus on preventive measures that deal with modifiable risk factors such as smoking, which continue to threaten progress in the management of HIV.

Current knowledge about tobacco-related mortality and morbidities warrants a holistic, biopsychosocial approach to managing people living with HIV. Incorporating smoking cessation services into the already established HIV clinics, to enable a multidisciplinary approach to addressing the complexity of social, psychological, and other health challenges faced by this special group of individuals, might be a practical approach. Encounters with PLWH during HIV clinic visits offer an opportunity to identify, educate and counsel current smokers about smoking cessation, and possibly initiate cessation treatments. Appropriate psychosocial support can also be provided during these encounters.

Only a few HIV-positive smokers are reported to be good candidates for a standard tobacco use cessation programme and tobacco use reduction, due to their special needs, which are caused by, among other factors, a lack of social support, and depression; therefore, cessation strategies should be adapted to this special population[4].

Other evidence shows that barriers to the provision of smoking cessation interventions are often organisational barriers, such as the absence of protocols, lack of educational material for patients, and the unavailability of pharmacological aids[19].

According to the American College of Cardiology, adding tobacco use status to the patient's problem list at every health encounter is recommended, to indicate the chronicity of this health

problem and the need for sustained attention [21]. Doing so will also alert the patient's other health care providers to reiterate smoking cessation advice at every encounter, and will facilitate coordination of tobacco treatment efforts across health providers[21].

1.3 SMOKING CESSATION GUIDELINES AND PHARMACOTHERAPY

The South African smoking cessation guidelines recommend both pharmacotherapy and behavioural treatments[17]. The Food and Drug Administration (FDA) approved nicotine replacement therapy products that include nicotine patches, lozenges, gums, inhalers and nasal sprays, as well as bupropion and varenicline for smoking cessation. The commonly recommended approach is the 5**A**s model, which involves five basic steps, namely (1) **A**sk about smoking status, knowledge about smoking risks and willingness to quit; (2) **A**lert the individual by asking whether they know about the benefits of quitting smoking and tell them that they can be helped; (3) **A**ssess their readiness to quit smoking; and (4 & 5) **A**ssist and **A**rrange smoking cessation intervention[22]. The Fagerström Tolerance Questionnaire[23] is a validated survey tool to measure symptoms of nicotine dependence (also see Appendix 2). A higher score correlates with severe nicotine dependence, which may increase the risk of relapsing from smoking cessation interventions. Unfortunately, not all these guidelines address smoking cessation measures tailored for PLWH, though much can be learnt from experience gathered on smoking cessation in HIV-negative individuals.

Pharmacological agents predominantly address acute nicotine withdrawal symptoms during the cessation process. Enhanced efficacy is achieved by employing dual nicotine replacement therapy agents – one as a 'controller' (e.g. a patch) and one as a 'reliever' (e.g. gum or spray)[24]. Bupropion – an antidepressant – appears to reduce long-term relapse and the undesired weight gain associated with cessation[25].

A nicotine receptor partial agonist that is available is varenicline (registered in South Africa as Champix). It acts as a partial agonist, thereby stimulating dopamine release and reducing nicotine withdrawal symptoms[26].

The complex drug interactions between ARV drugs and nicotine metabolism need to be borne in mind when smoking cessation is advised and pharmacotherapy instituted. These drug interactions may hinder the efficacy of nicotine replacement therapy. Nicotine metabolite ratio (NMR) is a biomarker that represents individual variation in the speed at which nicotine is metabolised. A higher NMR has been reported in PLWH on ART, compared to people who

are HIV negative. This report may be, in part, due to the interaction between nicotine metabolism and metabolism of some of the antiretroviral drugs[27]. Nicotine in tobacco is predominantly metabolised by hepatic cytochrome P450 2A6 (CYP2A6) and cytochrome P450 3A6 (CYP3A4), which also metabolise Efavirenz. Efavirenz, a non-nucleoside reverse transcriptase inhibitor, is one of the ARV drugs used to treat HIV. It induces CYP3A4 and has been associated with faster nicotine metabolism and a higher NMR. Transdermal nicotine patches supply a lower nicotine level and have been found to be ineffective in patients with a high NMR. All this may contribute to the difficulty faced by PLWH who attempt smoking cessation whilst using these products[27] therefore requiring dual nicotine replacement therapy.

Smokers may also be concerned about a decline in the quality of life following cessation, because they may view cessation as a disruption of their routine, or even as a loss of a coping strategy[6]. Evidence shows, however, that people who quit smoking actually lead more satisfied lives over the long term[28] – a finding that health care workers need to communicate to ameliorate fears or address barriers to quitting.

It is postulated that involving subjects (PLWH) themselves in a one-on-one smoking cessation programme is likely to have successful outcomes, as doing so will focus on the specific needs and challenges faced by each individual. The high prevalence of tobacco use, and low success rate of quitting poses a clinically significant problem for the overall health and quality of life of PLWH[29].

1.4 COVID-19 AND SMOKING

The COVID-19 pandemic has affected the whole world since the first case was reported in Wuhan, China, in December 2019[30]. Research about this infection and its complications has been ongoing across the world. Current research demonstrates higher COVID-19 mortality rates – up to 14 times higher – in smokers than in non-smokers[30]. As more evidence emerges regarding increased risk of severe COVID-19 for smokers, it becomes clear that more needs to be done to scale up smoking cessation programmes to assist individuals to quit smoking.

Smoking cessation rates after the start of the COVID-19 pandemic have been examined and found to be statistically higher than in the period prior to the pandemic[31]. The rate of smoking cessation was found to be 23.7% prior the COVID-19 pandemic, and it increased to 31.1% during the pandemic[32]. This higher cessation rate may offer an opportunity for implementing

effective smoking cessation efforts and supporting those who would wish to quit smoking during the COVID-19 pandemic, even amongst PLWH.

1.5 SMOKING CESSATION IN SOUTH AFRICA AND OTHER LOW AND MIDDLE-INCOME COUNTRIES

It has been reported that individuals who quit smoking before age 45 have the same life expectancy as non-smokers[32,33]. Individuals who continue to smoke beyond this age tend to die 10 years earlier than those who did not smoke[33]. Formal smoking cessation programmes exist in high-income countries, but not to the same extent in middle to low-income countries, such as South Africa. A single dedicated smoking cessation clinic in Groote Schuur Hospital in Cape Town is the only clinical service and training centre for tobacco treatment in the country[32]. Recently, in 2021, a smoking cessation clinic was established at the Helen Joseph Hospital in Johannesburg, though it is still in an early phase. These centres cater for all individuals who smoke and are not restricted to PLWH. Unfortunately, smoking cessation pharmacotherapy is not available for smokers who access public health services in South Africa[32]. Little is known regarding formal smoking cessation programmes provided in low-income countries, nor is data available on the applicability and assessment of cessation strategies that are applied in low-income countries, but developed in high-income settings [33,34].

Smoking cessation interventions for PLWH are necessary, particularly for historically underrepresented groups from poor socio-economic backgrounds[27]. More rigorous studies are also needed to assess intervention effectiveness and to increase the generalisability of findings[27], especially in countries with a high HIV prevalence, like South Africa.

This study aimed to establish why PLWH have not quit smoking, what their barriers to quitting are, and why previous attempts to quit have been unsuccessful. It also sought to highlight the need to seek sustainable methods to implement a successful smoking cessation programme by addressing specific barriers to quitting.

1.6 STUDY AIMS AND OBJECTIVES

The aim of this study was to assess and evaluate barriers to smoking cessation in people living with HIV.

The primary objective of the study was to describe barriers to smoking cessation amongst people living with HIV (PLWH) who attended an ART clinic at Chris Hani Baragwanath Academic Hospital (CHBAH) Adult HIV Clinic.

The secondary objectives were the following:

(1) To describe the demographic characteristics of this cohort, specifically within the following parameters: gender, age, socioeconomic and employment status, level of education (formal schooling completed or not);

(2) To determine the level of nicotine addiction according to the Fagerström test questionnaire.

(3) To determine individual willingness to quit smoking.

(4) To determine number of previous attempts to quit smoking.

(5) To identify barriers to successful attempts to quit smoking; and

(6) To assess knowledge of PLWH regarding available modalities to assist in smoking cessation.

1.7 METHODOLOGY

1.7.1 Study design

This was a prospective, questionnaire-based cohort study that analysed barriers to smoking cessation for adults living with HIV, and who smoke. The data was collected at CHBAH Adult Specialist HIV Clinic (Nthabiseng). The population comprised only patients who were smokers, i.e. cigarette smoking, and those using other concomitant illicit drugs, such as cocaine, marijuana or *nyaope* (a street drug in South Africa – a mixture of low-grade heroin, cannabis products, ARV drugs and other materials [35]). Concomitant alcohol use was also assessed. A questionnaire, in English, was issued to volunteering participants after consent had been obtained. The questionnaire comprised open and closed-ended questions. Participants who could not read or write were assisted by the main investigator and, where necessary, the questionnaire was translated verbally to the preferred language of participants, i.e. isiZulu or Setswana, to ensure that they understood all the questions and that their answers were captured properly. A total of 189 participants were completed the questionnaire.

1.7.2 Study setting

Nthabiseng Clinic is an established, specialised ART clinic at a tertiary institution (CHBAH) in Soweto, Johannesburg.

1.7.3 Study population and samples

The study participants were all adults above the age of 18 years who attended Nthabiseng clinic. Sampling was done in the waiting area of the clinic whilst all individuals attending the clinic on the day were waiting to be seen by a doctor. All eligible individuals were screened according to the inclusion criteria and those meeting the inclusion criteria were enrolled in the study. The individuals enrolled received an information pamphlet that was explained to them in their preferred language by the principal investigator. This was done in a private room, to ensure that participants were comfortable, and to ensure confidentiality.

1.7.4 Eligibility criteria

The inclusion criteria were the following:

(1) Individuals aged 18 years or older.

(2) HIV-positive and attending the CHBAH Nthabiseng Adult HIV Clinic; and

(3) Current smokers, including those currently attempting to quit smoking, those who had previously failed to quit, and those willing to quit smoking.

The exclusion criteria were the following:

(1) Individuals younger than eighteen years of age.

(2) Individuals who had already quit smoking.

(3) Non-smokers; or

(4) Individuals using snuff only.

1.7.5 Study tools

An anonymous questionnaire was administered to participants. The questionnaire comprised open and closed-ended questions, to assess the participants' knowledge of different modalities that can be used to help quit smoking, and information on the willingness to quit, previous attempts to quit and perceived reasons for unsuccessful attempts. A Fagerström questionnaire

was also used to assess the level of nicotine addiction. The questionnaire was administered by the primary investigator in the participants' preferred language of communication.

1.7.6 Data analysis

Data collection and cleaning were performed in Microsoft Excel. Data cleaning of numerical variables included investigating outliers and impossible values. Data cleaning of categorical variables included de-stringing of string variables and data reduction through creating meaningful categories. Data analysis was performed in Stata Version 15. Numerical variables were tested for normality using the Shapiro Wilk normality test. Normally distributed variables were described using means and standard deviations (SD), non-normal variables were described using the median and interquartile range (IQR). Categorical variables were described using frequencies and percentages. A histogram was used to present the age distribution in PLWH who smoke.

1.7.7 Ethics considerations

The study was carried out at CHBAH, Nthabiseng Adult HIV Specialist Clinic. Ethics approval was granted by the University of Witwatersrand Human Research Ethics Committee (M1911120). Permission to proceed with the study was also obtained from the hospital authorities.

Unique patient identification numbers were used on each questionnaire sheet to protect the identities of the study participants.

1.7.8 Funding

Costs were incurred through travelling and stationery (pens, paper, printing of questionnaires). Data analysis and scientific writing courses offered by the University of the Witwatersrand were attended; this training provided the knowledge needed to analyse data and write up the thesis. All expenses were covered by the principal investigator.

1.7.9 Study limitations

To run a successful programme to address smoking by people living with HIV, it is critical to address both patient and health care worker barriers. Health care worker barriers include time constraints, knowledge about available modalities and protocols to aid in smoking cessation, and the availability of smoking cessation guidelines. Health care provider attitudes and barriers in relation to addressing smoking cessation were not reviewed in this study.

As this was a questionnaire-based study, it relied on participants' self-reporting and honesty. No biomarkers were used to confirm honesty about smoking status.

This was a cross-sectional cohort questionnaire study and was only conducted at an ARV clinic during the stated period (see Table 1.1). It did not consider those patients who were seeking health care for other reasons, or elsewhere, therefore, this study only represents a population that is likely to be well and excludes those not attending the ARV clinic during the time of the study, either because they were hospitalised, not yet on ARVs, or not scheduled for a follow-up visit during the time of the study.

The study did not assess HIV control. HIV viral loads and CD4 counts were not obtained or considered.

COVID-19 and decreased access to health care facilities due to the pandemic may have skewed some of the data towards the end of the study.

1.7.10 Timing

Table 1.1: Gantt chart showing the timeline of the study

Activity	**Jan/Feb 2019**	**March 2019**	**April 2019**	**May 2019**	**June 2019**	**July/Aug 2019**	**Sep 2019**	**Oct 2019**	**Nov 2019**	**Dec 2019**
Literature review										
Preparing protocol										
Protocol assessment										
Ethics application										

Activity	**Jan/Feb 2020**	**March/ April 2020**	**May/June 2020**	**July/Aug 2020**	**Sep/Oct 2020**
Data collection			COVID pandemic	COVID pandemic	
Data analysis					
Writing up report					

CHAPTER 2: SUBMISSIBLE MANUSCRIPT

BARRIERS TO SMOKING CESSATION AMONGST PEOPLE LIVING WITH HUMAN IMMUNODEFICIENCY VIRUS (HIV) IN SOUTH AFRICA

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Abstract

Background: Antiretroviral therapy (ART) coverage in South Africa has improved the quality of life of people living with human immunodeficiency virus (PLWH). Smoking remains a major modifiable risk factor for non-HIV-related morbidity and mortality in this group of individuals.

Objective: To describe barriers to smoking cessation for people living with HIV who attended the Chris Hani Baragwanath Academic Hospital HIV clinic in Johannesburg, South Africa.

Methods: A voluntary, anonymous questionnaire was completed prospectively by 189 study participants who were smokers, and demographic and smoking-related data were collected. Nicotine dependence scores were formally evaluated using the Fagerström questionnaire for each study participant. Consent was obtained from all study participants.

Results: The mean age of participants was 45.37 years (standard deviation [SD] 11.77), with 85.19% (161/189) being men. Overall unemployment rate was 65.61% (124/189); 70.31% (133/189) had no matric qualification. The median number of years smoked was 19 (IQR 10–28 years) and the current median daily consumption was six cigarettes per day (IQR 4–10 cigarettes per day). The median Fagerström nicotine dependence score was 4 (IQR 2–5) – this is graded low to moderate nicotine dependence. There were no statistical differences in median Fagerström nicotine dependence scores by gender, age, employment or level of education. Overall, 179 (94.71%) individuals were willing to quit smoking, while 134 (70.90%) of the total study participants had previously attempted to quit smoking.

The majority of smokers living with HIV – 175 (92.59%) – were not familiar with smoking cessation pharmacotherapy. Of those who had previously attempted cessation, 93/134 (69.40%) reported stress as a reason for failed previous attempts to quit smoking, and 75/134 (55.97%) reported nicotine craving as a barrier to quitting. Overall, 36.51% (69/189) of study participants reported concomitant alcohol use.

Conclusion: A significant number of PLWH are not familiar with smoking cessation pharmacotherapy modalities that are available. Some of the self-reported barriers to quitting smoking were stress and nicotine cravings. As the majority of smokers living with HIV reported being willing to quit smoking, this offers an opportunity to offer smoking cessation services during each clinic follow-up visit and to educate smokers about the different smoking cessation modalities available, as well to offer psychosocial support.

2.1 INTRODUCTION

Now in its fourth decade, human immunodeficiency virus (HIV) remains a global pandemic, with an alarming spread in resource-limited countries, such as those in sub-Saharan Africa and South-East Asia[36]. In the year 2020, approximately 37.6 million people across the globe were living with HIV[37]. South Africa is a country with a high HIV infection rate, with an estimated overall prevalence of approximately 13.0% reported in the year 2020[37].The total number of people living with HIV (PLWH) in South Africa was estimated at approximately 7.8 million in the year 2020[38]. Increasing coverage of antiretroviral therapy (ART) in South Africa has improved the quality of life of PLWH and, hence, increased their survival and longevity[3].

Smoking is a modifiable risk factor for morbidity and mortality that may arise from smoking-related adverse effects. Tobacco use has been described as a major hurdle in the fight against HIV and AIDS[39]. More than twice as many life years are lost by PLWH who smoke than by the HIV-negative general population who smoke[40].The prevalence of current tobacco use in HIV-positive smokers in developed countries is estimated at between 40% and 74%[41–43].This is two- to threefold higher than in the general population, whose smoking rate is estimated at only 20%[41].

In South Africa, data on the prevalence of smoking by PLWH is limited, but prevalence ranges between 15% and 34%[3,44,45]. A Johannesburg-based study conducted in an HIV clinic found that 15% of PLWH self-described as current smokers, with more men than women smoking[44]. Another study, conducted in the North West and Western Cape provinces report prevalence of 34%[3] and 22%[45] respectively. Tobacco use remains high, and is on the rise in PLWH, and this trend requires scaled-up action to reduce the risk of tobacco-related diseases[3].

In the era of antiretroviral therapy (ART), good clinical outcomes achieved regarding the control of HIV may be threatened by the undesired complications related to tobacco use. Compared to the general population, lung malignancies occur at a younger age and after shorter exposure to smoking in PLWH[46]. More research is required to further understand the relationship between immunodeficiency (low CD4+ versus high CD4+ count) and lung cancer risk among HIV infected patients,

we plan to conduct additional more sophisticated analyses with time-updated modelling of

CD4 cell count. ART-adherent smokers were also found to be 6 to 13 times more likely to die from lung cancer than from traditional AIDS-related causes[47]. Smoking plays an important causal role in non-HIV-related illnesses that could lead to premature morbidity and mortality in PLWH[48].

Despite a call at the National Institutes of Health State-of-the-Science conference, for research to be done to evaluate tobacco control interventions in PLWH[16], only a few studies have been conducted to address this matter. Previous smoking cessation efforts have been aimed largely at the general population and it is unclear if these treatment strategies are suitable, effective or even applicable to cohorts with population-specific concerns and other clinical issues, such as PLWH[41].

Some of the perceived smoking cessation barriers reported in South Africa by PLWH include economic stressors, such as unemployment and poverty, and social or interpersonal stressors, such as lack of social support in particular due to having HIV[49]. Alcohol is also used as a coping mechanism to deal with stressful situations, and alcohol use frequently co-exists with smoking[49]. In this paper, we aim to describe barriers to smoking cessation facing PLWH, to assess knowledge about smoking cessation modalities, and their willingness to quit smoking.

2.2 METHODS

The study was conducted at Nthabiseng Clinic, which is an established, specialised ART clinic at a tertiary institution, the Chris Hani Baragwanath Academic Hospital (CHBAH), in Soweto, Johannesburg.

This was a prospective, questionnaire-based cohort study that assessed the barriers to smoking cessation facing adults living with HIV, and who smoke. The study population comprised all patients who were current cigarette smokers. An anonymous questionnaire was issued to volunteering participants after their consent had been obtained. A total of 189 participants were interviewed.

The inclusion criteria were the following:

(1) Individuals aged 18 years or older.

(2) HIV-positive and attending the CHBAH Nthabiseng Adult HIV Clinic; and

(3) Current smokers, including those currently attempting to quit smoking, those who had previously failed to quit, and those willing to quit smoking.

The exclusion criteria were the following:

(1) Individuals younger than 18 years of age.

(2) Individuals who have successfully quit smoking.

(3) Non-smokers; or

(4) Individuals using snuff only.

Participants who attended the clinic on the day of the study were randomly selected whilst they waited to be seen by a doctor. Those who admitted to using tobacco or smoking cigarettes were invited to voluntarily participate in the study by completing the questionnaire administered by the primary investigator in the participants' preferred language of communication. This was done in a private area to ensure confidentiality. The questionnaire assessed their knowledge of the different modalities that can be used to help people quit smoking, and enquired about their willingness to quit, previous attempts to quit smoking, perceived reasons for unsuccessful attempts and perceived barriers to smoking cessation. A Fagerström questionnaire was used to assess participants' level of nicotine addiction..

Completed questionnaires were captured in Microsoft Excel. Data cleaning and analyses were done in Stata Version 15. Data cleaning of numerical variables included investigating outliers and impossible values. Data cleaning of categorical variables included de-stringing of string variables and data reduction through creating meaningful categories. Numerical variables were tested for normality using the Shapiro Wilk normality test. Normally distributed variables were described using mean and standard deviations (SD); non-normal variables were described using medians and interquartile ranges (IQR). Categorical variables were described using frequencies and percentages.

Ethics approval was granted by the University of Witwatersrand Human Research Ethics Committee (M1911120). Permission to proceed with the study was also obtained from the hospital authorities. Unique patient identification numbers were used on each questionnaire sheet to protect the identity of the study participants.

2.3 STUDY FINDINGS

2.3.1 Description of PLWH who smoke enrolled in the study

Between 28 January 2020 and 26 February 2021, a total of 189 PLWH who smoke were enrolled in the study. The majority were men 161 (85.2%), Black (99.47%), and unemployed (65.61%), and did not have a matric qualification (70.37). Age followed a normal distribution, with a mean age of 45.37 years (SD 11.77 years). Figure 1 represents age distribution in PLWH who smoke, Table 2.1 presents the demographic characteristics of participants who were enrolled in the study.

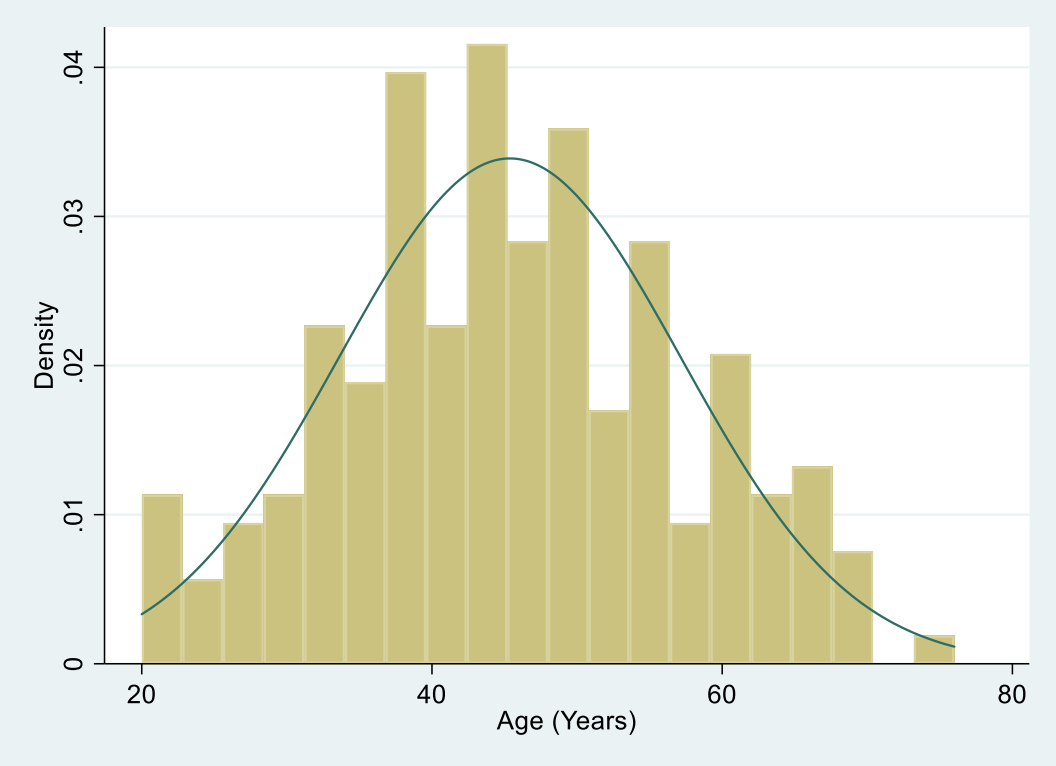


Figure 1: Distribution of age in PLWH who smoke

Age followed a normal distribution, with a mean age of 45.37 years (SD 11.77).

Table 2.1: Demographic characteristics of PLWH who smoke (N=189)

Characteristic	N	%	Mean (SD)
Age			45.37 (11.77)
Gender			
Male	161	85.19	
Female	28	14.81	
Race			
Black	188	99.47	
Mixed race	1	0.53	
Employment			
Unemployed	124	65.61	
Formally employed	33	17.46	
Informally employed	25	13.23	
Retired	7	3.70	
Education			
Matric	44	23.28	
University	12	6.35	
No matric	133	70.37	

2.3.2 Levels of nicotine addiction according to the Fagerström test

Most PLWH smoked filtered cigarettes (88.4%). The median number of cigarettes smoked per day was 6 (IQR 4–10) and the median number of years smoked was 19 (IQR 10–28). The median number of pack years was 5 (IQR 2.5–13). The level of nicotine addiction in PLWH who smoked was moderate, with a median Fagerström score of 4 (IQR 2–5) (Table 2). There were no statistical differences in median Fagerström score by gender, age, employment and level of education. Table 2.2 presents the level of nicotine addiction

Table 2.2: Level of nicotine addiction

Characteristic	N	%	Median (IQR)
Type of cigarette			
Filtered	160	88.40	
Unfiltered	21	11.60	
Number of cigarettes per day			6 (4–10)
Number of years smoked			19 (10–28)
Pack years*			5 (2.5–13)
Fagerström score			4 (2–5)

* Pack years were calculated as (number of cigarettes per day/20) x number of years smoked

2.3.3 Willingness to quit smoking and previous attempts at smoking cessation

Nearly all (n=179; 94.71%) patients were willing to quit smoking and over 70% had previously tried to quit (Table 2.3). The median attempts to quit were 2 (IQR 1–3). While the majority did not specify their reasons for wanting to quit smoking, the commonest specified reason was for health reasons. A combination of pharmacotherapy and counselling was the most preferred method of assistance (n=77; 40.74%), while a third of patients preferred pharmacotherapy alone and 12.17% preferred counselling only. Reasons for failed smoking cessation included stress (49.21%), cravings (39.68%) and depression (7.41%).

Table 2.3: Readiness to quit and willingness to quit smoking

Characteristic	**N (%)**
Willingness to quit smoking	
Yes	179 (94.71%)
No	8 (4.23%)
Not specified	2 (1.06%)
Previous attempts to quit	
Yes	134 (70.90%)
No	53 (28.04%)
Not specified	2 (1.06%)
Reasons for wanting to quit	
Health reasons	13 (6.88%)
Financial	3 (1.59%)
Bad nicotine odour	1 (0.53%)
Personal choice	1 (0.53%)
Not specified	171 (90.48%)
Preferred method of assistance	
Both pharmacotherapy and counselling	77 (40.74%)
Pharmacotherapy	62 (32.80%)
Counselling	23 (12.17%)
Any	25 (13.23%)
Reasons for failed attempt at quitting	
Stress	93 (49.21%)
Cravings	75 (39.68%)
Depression	14 (7.41%)
Fear of lack of coping mechanisms	7 (3.70%)

Characteristic	N (%)
Mental health disorders	5 (2.65%)
Lack of social support	5 (2.65%)
Anxiety	5 (2.65%)
Lack of health care worker support	5 (2.65%)
Cost of medication or quitting assistance	1 (0.53%)
Concomitant alcohol use	4 (2.12%)
Habit	2 (1.06%)
Smoking for fun	1 (0.53%)
Peer pressure	1 (0.53%)

2.3.4 Perceived barriers to quitting smoking

Perceived barriers to smoking cessation included concomitant drug use, such as marijuana (30.16%), cocaine (1.06%), *nyaope* (1.59%) crystal meth (1.59%), Mandrax (0.53%) and snuff (0.53%). Common sources of stress were financial (49.74%), chronic illness (20.11%) and interpersonal relationship difficulties (17.99%). Table 2.4 breaks down the data relating to these barriers.

Table 2.4: Perceived barriers to quitting smoking

Characteristic	N	%
Concomitant drug use		
Marijuana	57	30.16
Cocaine	2	1.06
Nyaope	3	1.59
Other, specify		
Crystal meth	3	1.59
Mandrax	1	0.53

Snuff	1	0.53
Alcohol use		
None	84	44.44
Any i.e. including Occasional	69	36.51
Stress		
Financial	94	49.74
Chronic illness	38	20.11
Interpersonal	34	17.99
Unemployment	2	1.06
*Other**	11	5.83(0.53% each)

* Other included the following: unemployment, family problems, self-esteem and well-being, lack of quitting assistance, lost both parents, future uncertainty, divorce, home circumstances, poor living conditions (overcrowding at home), and failure to reach personal goals.

2.3.5 Knowledge of modalities available to assist in smoking cessation

The majority of participants (n=175; 92.59%) were not familiar with any smoking cessation modalities. Only 7.41% had ever heard of nicotine replacement therapy, one person (0.53%) knew about counselling as a smoking cessation modality and one person was aware of the use of tricyclic antidepressants. None of the patients had ever heard of the use of varenicline, bupropion or Wellbutrin as a smoking cessation modalities. Table 2.5 demonstrates knowledge of quitting modalities.

Table 2.5: Knowledge of quitting modalities

Characteristic	N	%
Not familiar with smoking cessation modalities	175	92.59
Nicotine replacement therapy	14	7.41
Non-pharmacological therapy (e.g. counselling)	1	0.53
Tricyclic antidepressants	1	0.53
Varenicline	0	0.00
Bupropion/Wellbutrin	0	0.00

2.4 DISCUSSION

Globally, a total number of 1 397 million people aged 15 years and over consumed a tobacco product in the year 2000[36]. Over 8 million tobacco-related deaths occur every year globally, and this figure is projected to rise to approximately 10 million deaths per year by 2030[36,37]. On the African continent, highest smoking rates are reported for South Africa, with higher rates among people who are poorer, less educated and male[38,40]. Furthermore, 31% of South Africans aged 15 years and older report smoking tobacco[41].

Despite the adverse health effects of smoking, the prevalence of smoking among PLWH is up to three times greater than those observed in the general population[42]. A higher prevalence of smoking, of more than 40%, is reported by the 2005–2011 National Survey on Drug Use and Health (NSDUH) data[42] and prior reports on smoking in PLWH show even a higher prevalence of between 50–70%[43,46–48,50,51]. The prevalence of smoking amongst PLWH in South Africa ranges between 15% and 34%[3,13,38].

Smoking accounts for 12% of deaths of men, and 6% of deaths of women in the general population globally[45] and is ranked second among the 10 leading mortality risk factors in the world[52]. Some of the smoking-associated diseases include lung cancers, respiratory and cardiovascular diseases[52,53], all of which have poor health outcomes in PLWH. In addition, PLWH have a more than twofold higher incidence than the general population of non-AIDS-related morbidity due to cancer and myocardial infarctions[44]. Up to 70% of myocardial infarctions[49] and 27% of cancers[54] in PLHIV are attributable to smoking. PLWH lose

more life years to smoking than to HIV and its complications; furthermore, smoking is associated with 12.3 years life lost, compared to 5.1 years life lost due to just the HIV status[6].

This study highlights the challenges faced by PLWH who suffer from nicotine dependence in resource-limited health facilities in South Africa. Previous research indicates that smokers engage in more health-risk behaviours and fewer health-promoting behaviours relative to non-smokers[55,56]. A study in South Africa involving PLWH found an association between alcohol use and smoking by men[3]. In our study, we report concurrent health-risk behaviour in the form of alcohol and marijuana use. In most cases, alcohol was being used as a coping mechanism for stress, and it frequently co-occurs with smoking[15].

Other studies involving PLWH in developed countries report alcohol and other substance use, stress, use of smoking as a coping mechanism to deal with the HIV status, and the perceived burden of taking medication for smoking cessation in addition to HIV medication as barriers to smoking cessation[57–59].The first study conducted in South Africa in 2018 found barriers occurring at the economic, social/interpersonal, and individual levels to be responsible for inducing stress, which then hinders smoking cessation[15]. These findings are similar to those of our study, which found a high rate of unemployment and, therefore, no source of income, which aggravates the stress and therefore the use of alcohol, which co-occurred with smoking, as a coping mechanism for PLWH.

In our study, an overwhelming majority of patients indicated their wish to quit smoking; however, most were not familiar with smoking cessation strategies, including pharmacotherapy. This finding is similar to that of a study done in Johannesburg, South Africa, which found a strong willingness to quit smoking; however, unlike our study, participants in that study knew about smoking cessation strategies, but did not have knowledge of resources that they could access for assistance and advice[13]. Some of the factors that may have contributed to this difference between the studies are the differing demographics of participants in the two studies, such as gender, race and socio-economic status; in our study-the majority of participants were from low socio-economic class and had a lower level of education. During the current coronavirus 2019 disease (COVID-19) pandemic, people report a willingness to quit smoking, as they fear the risks associated with COVID-19 and smoking[60]. Our study did not assess this trend, though it may offer an opportunity to implement and scale up smoking cessation services at this time.

Although further work is needed to assess the efficacy of integrating smoking cessation services in already established ART clinics in sub-Saharan Africa, a previous study done in Uganda suggests that integrating smoking cessation counselling into routine clinical care may decrease smoking among PLWH[61].

The Fagerström Test for Nicotine Dependence, which is used extensively in various countries, is a screening questionnaire for assessing the nicotine dependence of smokers. Previous analysis of its use had confirmed its reliability for the assessment of nicotine dependence in different settings and populations[62]. A lower Fagerström score is associated with a lower level of nicotine dependence, and a higher score with a higher level of nicotine dependence and higher rates of nicotine withdrawal symptoms when attempting to quit smoking. The rate of smoking abstinence has been noted to be higher in individuals with lower Fagerström Test scores for nicotine dependence and, furthermore, nicotine dependence may influence the cost-effectiveness of smoking cessation programmes[63]. In our study, the median Fagerström score of 4 (which is regarded low to moderate) might offer an opportunity for a successful, cost-effective smoking cessation intervention.

2.5 CONCLUSION

In conclusion, in order to improve overall care of PLWH, modern HIV care should include strategies to assist individuals who smoke to quit[51]. In South Africa, there is insufficient data regarding cigarette smoking prevalence by PLWH[13], and therefore, more research is required to assess the barriers to smoking cessation, particularly the health care worker barriers to offering smoking cessation support and services. Research is also required to assess the feasibility of implementing a smoking cessation intervention programme amongst PLWH, particularly in resource-limited settings. An ideal, cost-effective and convenient model would be to incorporate such services into the already established ART clinics, to improve holistic patient care and provide continuity of care in addressing this modifiable health-risk behaviour, which has been noted to be most prevalent in PLWH.

A study conducted at a dedicated smoking cessation clinic in Cape Town, South Africa, found that moderate levels of nicotine dependence coexist with significant depression and anxiety symptoms, it further suggested that psychological/behavioural support focusing on depressive symptoms may be a greater priority than simple pharmacotherapy [29]. Our study highlighted

the lack of knowledge by PLWH regarding the available smoking cessation modalities. A focused smoking cessation strategy should seek to address barriers uncovered in this study.

2.6 STUDY LIMITATIONS

Health care provider attitudes and barriers to addressing smoking cessation were not reviewed in this study.

As this is a questionnaire-based study, it relied on participants' self-reporting and recall.

This was a cross-sectional cohort questionnaire study and was only conducted at one ARV clinic at the particular time. It did not consider PLWH who sought health care for other reasons, or elsewhere, therefore, this study represents a population more likely to be well and excludes those not attending the ARV clinic at the time of the study – either because they were hospitalised, not yet on ARVs, or not scheduled for a follow-up visit at the time of the study.

The study did not take into consideration HIV control. Participants' viral load and CD4 counts were not obtained or considered in this study. COVID-19 and decreased access to health care facilities due to the pandemic may have skewed some of the data collected towards the end of the study. The pandemic may have changed health-seeking behaviour and, therefore, skewed data to include people who are generally health conscious, more likely to seek health advise and more likely to want to quit smoking.

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CHAPTER 3: APPROVED PROTOCOL

TOPIC: BARRIERS TO SMOKING CESSATION AMONGST PEOPLE LIVING WITH HUMAN IMMUNE DEFICIENCY VIRUS IN SOUTH AFRICA

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INTRODUCTION

In its fourth decade, human immune deficiency virus (HIV) remains a global pandemic an alarming spread in resource-limited countries, like those in sub-Saharan Africa and South-east Asia(1). According to the United Nations Programme on HIV/AIDS, approximately 36.9 million people worldwide were living with HIV/acquired immune deficiency syndrome (AIDS) in 2017.

South Africa is one of the countries in the world with a high HIV infection rate, with an estimated overall prevalence of approximately 13.1%(2).The total number of people living with HIV (PLWH) in South Africa was estimated to be approximately 7.52 million in 2018(2). Increasing antiretroviral therapy (ART) coverage in South Africa has improved the quality of life amongst PLWH and, hence, increased survival and longevity(3). This is evidenced by an increasing prevalence of HIV, as those infected continue to live longer and have near-normal life expectancies(4).

Smoking has been described as a major hurdle in the fight against HIV and AIDS(5). HIV-infected smokers on ART lose more life-years to smoking than to HIV-related complications. More than twice as many years of life are lost in PLWH who smoke, in comparison to members of the HIV-negative general population who smoke(6).

The prevalence of current tobacco use in HIV-positive smokers is estimated at between 50 and 70%(7). This is higher than the general population, which is estimated at only 20%(7). In the era of antiretrovirals (ARVs), good clinical outcomes achieved in the control of HIV may be threatened by the undesired complications of tobacco. Smoking-related cardiovascular, pulmonary and neoplastic diseases are on the rise in this group of individuals (PLWH).

Case-control studies show that acute coronary syndrome is nearly twice as high in PLWH who smoke compared to HIV-negative controls(8).

Compared to the general population, lung malignancies occur at a younger age and after shorter exposure to cigarettes in PLWH(9). ART-adherent smokers were found to be 6 to 13 times more likely to die from lung cancer than from traditional AIDS-related causes(10). Smoking plays an important causal role in non-HIV-related illnesses, leading to premature morbidity and mortality in PLWH(11) and smoking, hence, remains a critical modifiable risk factor.

A national downward trend in smoking levels has been reported in the general population in South Africa since the introduction of control measures for smoking in public areas(12).

Tobacco use remains high and is on the rise in PLWH, and requires scaled-up action to reduce the risk of a range of tobacco-related diseases(3).

Despite a call for research at the National Institutes of Health State-of-the-Science conference to evaluate tobacco control interventions in PLWH(13), only a few studies have been conducted to address this issue. Unfortunately, smoking cessation programmes have not been a priority in the management of HIV. More work needs to be done to study the extent of tobacco use among people living with HIV in low-income and middle-income countries. In South Africa, a Johannesburg-based study conducted in an HIV clinic found 15% PLWH to be self-described current smokers, of whom more were men than women(14). Analysis of data from 28 low and middle-income countries on tobacco use amongst PLWH reports a higher prevalence of smoking amongst HIV-positive men than HIV-positive women(15).

Smoking cessation efforts have largely been aimed at the general population and it is unclear if these treatment strategies are suitable, effective or even applicable to cohorts with population-specific concerns and other clinical issues, such as PLWH(7). Some of the perceived smoking cessation barriers reported locally in South Africa amongst PLWH include economic stressors, such as unemployment and poverty, and social or interpersonal stressors, such as lack of social support due to being HIV positive(16). Alcohol is also used as a coping mechanism to deal with stressful situations and frequently co-occurs with smoking(16).

Smoking prevalence among PLWH in South Africa, in particular, is alarmingly high, yet high-quality evidence on interventions for smoking cessation is not available(5).A cross-sectional survey study done in the North West province of South Africa reports a strong association between current smoking and use of other harmful substances, like marijuana(3). This is seen as one of the contributing reasons for smoking cessation being successful or why people are reluctant to quit smoking. PLWH who continue to smoke benefit from ART, and later suffer the consequences of tobacco-related morbidity and mortality.

The current knowledge of tobacco related mortality and morbidities warrants a holistic, biopsychosocial approach in managing people living with HIV. Smoking cessation centres need to be incorporated into HIV clinics or centres, bearing in mind the complexity of social, psychological, and other health challenges faced by this group of individuals. Encounters with PLWH during follow up at HIV clinics offer an opportunity to identify and engage current smokers who are willing to quit smoking, to initiate cessation treatments, and facilitate appropriate follow-up and support.

Only a few HIV smokers are reported to be good candidates for a standard tobacco use cessation programme and tobacco use reduction due to their special needs, i.e. lack of social support, depression, etc. Cessation strategies should therefore be adapted to this special population(3).

Previous findings in health care services and implementation research have provided some insight into frequent barriers to the provision of smoking cessation interventions, some of which include organisational barriers, such as the absence of protocols, educational material for patients, and/or pharmacological aids(15).

According to the American College of Cardiology, adding tobacco use status to the patient's problem list at every health encounter is recommended, to indicate the chronicity of this health problem and a need for sustained attention. This will also alert the patient's other health care providers to reiterate smoking cessation advice at every encounter, and will facilitate coordination of tobacco treatment efforts across health providers(17).

The South African smoking cessation clinical practice guidelines published in 2013 are based on published evidence and international guidelines from the US Centers for Disease Control, the American College of Chest Physicians, the UK National Institute for Clinical Excellence and the Cochrane Collaboration Database of Systematic Reviews for all topics relating to tobacco smoking(18).

The South African smoking cessation guidelines recommend both pharmacotherapy and behavioural treatments. The approved nicotine-replacement-therapy products of the Food and Drug Administration (FDA) include nicotine patches, lozenges, gums, inhalers, nasal sprays and bupropion and varenicline for smoking cessation. The commonly recommended approach is the 5As model, which involves 5 basic steps. The Fagerström Tolerance Questionnaire is a validated survey tool to measure symptoms of nicotine dependence – a higher score correlates with severe nicotine dependence, which may increase risks of relapsing from smoking cessation interventions. Unfortunately, none of these guidelines address smoking cessation measures tailored for PLWH.

Pharmacological agents predominantly address acute nicotine withdrawal symptoms during the quitting process. Enhanced efficacy is achieved by supplementing dual nicotine replacement therapy agents with one acting as a 'controller' (e.g. a patch) and another one as a 'reliever'

(e.g. gum or spray)(19). Bupropion, an antidepressant, appears to reduce long-term relapse and the undesired weight gain associated with quitting(20).

A nicotine receptor partial agonist that is available is varenicline (registered as Champix in South Africa). It acts as partial agonist, thereby stimulating dopamine release and reducing nicotine withdrawal symptoms(21).

Smokers may also be concerned with a decline in quality of life following cessation, simply because they view smoking cessation as a disruptor of routines and relationships, or even a loss of coping strategies(5). Growing evidence shows that those who quit, over the long term, actually lead more satisfied lives(22) – a finding that health care workers need to disseminate in order to ameliorate fears or barriers to quitting.

The complex interaction between ARV drugs and nicotine metabolism needs to be considered for PLWH who try to stop smoking. These drug interactions may hinder the efficacy of nicotine replacement therapy. Nicotine metabolite ratio (NMR) is a biomarker that represents individual variation in the speed that nicotine is metabolised. A higher NMR has been reported in PLWH, compared to people who are HIV negative. This phenomenon is explained by the complex interaction between nicotine metabolism and some ARV drugs(23). The nicotine present in tobacco is predominantly metabolised by hepatic cytochrome P450 2A6 (CYP2A6) and cytochrome P450 3A6 (CYP3A4), which also metabolise most ARV drugs. Efavirenz, a non-nucleoside reverse transcriptase inhibitor that is used in the treatment of HIV, induces CYP3A4 and has been associated with faster nicotine metabolism and a higher NMR. Transdermal nicotine patches have been found to be ineffective in patients with a high NMR, thereby contributing to the difficulty faced by these individuals to quit smoking whilst using these products(23).

Involving PLWH themselves is likely to yield successful outcomes for smoking cessation programmes, as doing so will focus on their specific needs and challenges. The high prevalence of tobacco use and low success of quitting remains a clinically significant problem for the overall health and quality of life of PLWH(24).

In conclusion, smoking cessation interventions have not been widely implemented in the public health sector in South Africa, and to the best of our knowledge, there are currently no programmes or centres addressing smoking cessation specifically in PLWH in the Gauteng region. More work needs to be done to guide the establishment of such a programme. It is,

therefore, the aim of this study to answer some of the questions relating to why PLWH have not stopped smoking, why previous attempts to stop have been unsuccessful, and which sustainable methods for a successful smoking cessation programme can be incorporated into ARV clinics.

More smoking cessation interventions for PLWH are necessary, particularly for historically under-represented groups(23). More rigorous studies are also necessary to improve assess to interventions effective, and to increase the generalisability of findings(23), especially in countries with high a HIV prevalence, like South Africa.

STUDY OBJECTIVES

Primary Objective

To describe barriers to smoking cessation in people living with HIV (PLWH) attending an ARV therapy clinic at Chris Hani Baragwanath Academic Hospital Adult HIV Clinic.

Secondary Objectives (applicable to PLWH who smoke)

1. To describe the demographic characteristics of this cohort, including gender, age, socioeconomic status, level of education (formal schooling completed or not);
2. To determine the level of nicotine addiction according to the Fagerström test;
3. To determine individual willingness to stop smoking;
4. To determine number of previous attempts to stop smoking;
5. To identify barriers to successful attempts to quit smoking; and
6. To assess knowledge of PLWH regarding modalities available to assist in smoking cessation.

METHODS

This will be a prospective, questionnaire-based cohort study that will analyse barriers to smoking cessation in adults living with HIV who smoke. The study will be based primarily at the Chris Hani Baragwanath Academic Hospital Adult HIV Clinic. Should the the targeted number of study participants not be reached, the study will be expanded to Helen Joseph Hospital and Charlotte Maxeke Academic Hospital Adult HIV clinics. The study will include all patients who are current smokers: whether they smoke cigarettes, marijuana or *nyaope*,

whether they vape, and if they use concomitant illicit drugs. A questionnaire with open and closed-ended questions will be administered confidentially to all eligible individual patients. Where applicable, patients who cannot read or write will be assisted by the principal investigator (myself) and a recruiting clerk from Wits Research. A minimum of 200 patients will be interviewed. Our aim is to recruit a total of 250 patients.

INCLUSION CRITERIA

The following individuals will be assessed:

1. Individuals eighteen years or older;
2. HIV positive and attending an HIV clinic; and
3. Patients who smoke or use tobacco, current tobacco users, individuals struggling or willing to stop smoking.

EXCLUSION CRITERIA

1. Individuals younger than eighteen years of age;
2. Patients who have quit smoking; or
3. Non-smokers.

DATA ANALYSIS

NVivo data analysis software will be used. Quantitative variables will be described as mean ± standard deviations, while qualitative variables will be described as percentages. Frequency proportion tables will be used for quantitative data. Quantitative chi-square tests will be used for comparing categorical variables, and P value will be used to assess associations. T-Test will be used to compare different outcomes for continuous categorical variables.

ETHICS

The research proposal is to be submitted to the University of Witwatersrand Human Research Ethics Committee for approval.

The research will be registered with the National Health Research Database.

FUNDING

Costs mainly relate to stationery (pens and paper, as well as printing of questionnaires, i.e. toner, paper and staples). Costs will be minimal and will be covered by the principal investigator.

STUDY LIMITATIONS

1. In order to run a successful programme to address smoking by PLWH, it is critical to address barriers originating with both patients and health care workers. Health care worker barriers include time constrains, knowledge of available modalities to aid in smoking cessation, and guidelines. Health care provider attitudes and barriers towards addressing smoking cessation will not be reviewed by this study.

2. As this is a questionnaire-based study, it will rely on participants' self-reporting and honesty. No biomarkers will be used to confirm honesty about smoking status.

3. This will be a cross-sectional cohort questionnaire study, and it will only be conducted at an ARV clinic during the stated period. It will only consider those patients who seek health care and taking ARV at that time. This limitation may represent a population more likely to be well, and exclude those not attending the ARV clinic at that time, either because they are hospitalised, because they are not yet on ARVs, or are not scheduled for a follow up visit at the time the study will take place.

4. The study will not take into consideration the HIV virological control and immunological status of participants in the form of CD4+ counts and HIV viral loads.

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Appendix 1: Timing of research

Appendix 2: Fagerström test

Appendix 3: Participant questionnaire

Appendix 4: Participant consent form

Appendix 5: Participant information leaflet

Appendix 1: Timing of research

Activity	Jan/Feb 2019	March 2019	April 2019	May 2019	June 2019	July/Aug 2019	Sep 2019	Oct 2019	Nov 2019	Dec 2019
Literature review										
Preparing protocol										
Protocol assessment										
Ethics application										

Activity	Jan/Feb 2020	March/ April 2020	May/June 2020	July/Aug 2020	Sep/Oct 2020
Data collection			COVID pandemic	COVID pandemic	
Data analysis					
Writing up report					

Appendix 2 Fagerström Test for Nicotine Dependence

PLEASE TICK {□) ONE BOX FOR EACH QUESTION

How soon after waking do you smoke your first cigarette?	Within 5 minutes 6-30 minutes 31-60 minutes After 60 minutes	□3 □2 □1 □0
Do you find it difficult to refrain from smoking in places where it is forbidden? e.g. Church, Library, etc.	Yes No	□1 □0
Which cigarette would you hate to give up?	The first in the morning Any other	□1 □0
How many cigarettes a day do you smoke?	10 or less 11 - 20 21 - 30 31 or more	□0 □1 □2 □3
Do you smoke more frequently in the morning?	Yes No	□1 □0
Do you smoke even if you are sick in bed most of the day?	Yes No	□1 □0

Total Score

SCORE 1- 2 = low dependence 5 - 7= moderate dependence

3-4 = low to mod dependence 8 + = high dependence

Add up the scores from the questionnaire.

Appendix 3: Anonymous questionnaire

HEALTH HISTORY QUESTIONNAIRE

All questions contained in this questionnaire are strictly confidential and will become part of your medical record

Study number: ☐ M ☐ F	Age (years) :
Ethnicity: ☐ Black ☐ Caucasian ☐ Mixed race ☐ Asian ☐ Other	
Employment: ☐ Formally Employed ☐ Informally employed ☐ Unemployed ☐ Retired	
Highest Level of Education: ☐ No Matric ☐ Matric ☐ University	

FAGERSTRÖM SCORE

SMOKING STATUS	
☐ Current ☐ Previous ☐ Never ☐ Passive smoking	
Number of cigarettes per day:	Number of years smoked:
Pack year history:	
Type of Cigarettes (please tick): Filtered Unfiltered Counterfeit Legal	
Previous attempts to quit: ☐ Yes ☐ No If yes, number of attempts to quit	

Are you familiar with any smoking cessation modalities (Choose whichever is applicable to you) ☐ Nicotine Replacement therapy ☐ Non-Pharmacological therapy i.e. counselling etc. ☐ Buproprion/Wellbutrin ☐ Champix ☐ Tricyclic Antidepressants ☐ Other, please specify……. ☐ Not Familiar with any modalities
Reasons to failed attempts at quitting: Please tick whichever is applicable ☐ Mental health care disorders ☐ Stress ☐ Lack of social support ☐ Cravings ☐ Anxiety ☐ Lack of health care worker support ☐ Cost of medication/quitting assistance ☐ Depression ☐ Fear of lack of coping mechanisms ☐ Other, please specify……..

READINESS TO QUIT	
Do you wish to stop smoking?	☐ yes ☐ no Please provide reason why
If motivated to stop, please provide preferred method of assistance	None ☐ Any ☐
Please tick whichever is applicable	☐ Counselling ☐ Pharmacotherapy ☐ Both

	☐Other, please specify……

PERCEIVED BARRIERS TO QUITTING	
Alcohol use	None ☐ Any ☐ If any, please indicate units per week consumed:
Stress	Interpersonal Financial Chronic illness Other, please specify

Other perceived barriers, please specify below