# The association between substance use and HIV in two Sub-Saharan African countries, 2014 - 2016

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# Abstract

## Background

People Living With HIV/AIDS (PLWHA) are recognized to have an increased risk of substance abuse - alcohol heavy episodic drinking (HED), tobacco smoking, and illicit drugs. Substance use amongst PLWHA is associated with poorer antiretroviral treatment (ART) adherence, increased risk of cancers, and worse morbidity and mortality. Substance use is also associated with an increased risk of HIV infection amongst those who are HIV negative. The majority of this research is focused outside of the African continent and in high-income countries; thus, this study aims to contribute towards research in low-middle income African countries such as South Africa and Kenya.

## Aim

This study aims to investigate the association between HIV and substance use in South Africa and Kenya, and the possible associated covariates.

## Methods

The study population for this secondary data analysis included n=7919 men and women participants drawn between the ages of 40 and 60 recruited between August 2013 and August 2016. The Mann-Whitney test was used for continuous variables and all other categorical variables were analysed using a chi squared test or Fisher's exact test. Predictive factors for the logistic regression models were informed by the literature review and conceptually modelled using a Direct Acyclic Graph. An overall logistic regression model was run which included both countries, and then separate logistic regression models were run for Kenya and South Africa.

## Results

The prevalence of substance use in the overall sample was 54.30%. In Kenya it was 51.33% and in South Africa (SA) 55.60%. The prevalence of HIV in the overall sample was 20.94%. In Kenya HIV prevalence was 13.66%, and in SA 23.35%. PLWHA had a 1.22 greater odds of substance use than those who were HIV negative in the overall sample (p=0.012, 95%CI 1.04 - 1.43). In Kenya, PLWHA had a 1.49 higher odds of substance use (p=0.013, 95%CI 1.09 - 2.03). In SA, there was no significant association found between HIV status and substance use. In the Kenyan logistic model HIV status, sex, marital status and employment status were found to be associated with substance use. Full-time employment and marriage presented as protective factors against substance use in Kenya. In the SA logistic model age, sex, marital status and employment status were associated with substance use. Marriage was also a protective factor for the SA model. Self-employment and informal employment increased the odds of substance use by more than two-fold in the SA model (aOR=2.27, p<0.001, 95%CI 1.63-3.16; aOR= 1.50, p=0.0008, 95%CI 1.19-1.91 respectively). The factor with the largest odds for substance use across all three models was being male, with increased odds of 15.5 in the overall model (p<0.0001, 95%CI 13.4-17.9), 11.6 in Kenya (p<0.0001, 95%CI 8.65-15.5) and 17.7 in South Africa (p<0.0001, 95%CI 14.9-21.1).

## Conclusion

Treatment of substance use disorders should become a staple in integrated routine ART care as the prevalence of substance use in PLWHA in this study and across the literature is high, especially in men The implementation of the substance use treatment should be tailored to the unique gendered and socioeconomic factors that are present in each country.

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# CHAPTER 1

This chapter consists of a background introduction (section 1.1) to the broader topic of HIV prevalence estimates and incidence rates in Sub-Saharan Africa (SSA), with a key focus on South Africa and Kenya. The background covers the link between substance use and HIV drawing on global literature, it then briefly presents a few key definitions (1.1.1), before moving on to a more in-depth literature review. The literature review (1.2) first covers the current landscape of HIV and substance use in SSA (1.2.1), before exploring Kenya (1.2.2) and South Africa (1.2.3) in detail as sub-sections. Specifically, the literature review focuses on tobacco use, alcohol consumption and drug use in these two countries, as these two countries are the focus for this research report. Finally, a special section of the literature review is dedicated to the gendered dynamics of substance use (1.2.4). The chapter concludes with the research problem statement (1.3) and the aim of the study (1.4).

## 1. INTRODUCTION

### 1.1 Brief Background

At the end of 2022 it was estimated by the World Health Organisation (WHO) that globally approximately 39 million People were Living With HIV/AIDS (PLWHA) (WHO, 2023). Of this global disease burden, Sub-Saharan Africa (SSA), and more specifically the Eastern and Southern African region carries majority of this burden (UNAIDS, 2023; WHO, 2023).

The WHO Eastern and Southern African region contains half (52%) of the world's PLWHA population, accounts for 37% of all new global HIV infections and 38% of all HIV-related deaths in 2022 (WHO, 2023). South Africa is of particular interest to the global HIV landscape as it contains the largest population of PLWHA in the world (Simbayi et al., 2019) with 7.6 million PLWHA as of 2022 (UNAIDS, 2022b).

Kenya is also important on the global HIV stage as it contains one of the largest populations of PLWHA in the Eastern Africa region with a reported 1.4 million as of 2022 (UNAIDS, 2022a).These two countries are the focus of the research report.

Within South Africa, the national prevalence of HIV was last estimated to be 14.0%, with women and people aged 25-49 years disproportionately affected (Simbayi et al., 2019). In Kenya, the latest released national prevalence estimate among adults was 4.9%, with women and people aged 50-64 years disproportionately affected compared to men and other age groups (Kenyan Ministry of Health, 2022).

South Africa's Fifth National HIV Prevalence, Incidence, Behaviour and Communication Survey (SABSSM V) stated that SA's overall incidence rate was 0.48% (Simbayi et al., 2019). At the time of writing this research report, the SABSSM VI report has not yet been released to the public by the South African government. The latest published Kenya Population based HIV Impact Assessment (KENPHIA) reported their 2018 HIV incidence rate at 0.14% for ages 15-64 years (Kenyan Ministry of Health, 2022).

Substance use (i.e., particularly alcohol heavy episodic drinking, injectable drug use, and non-injectable drug use) in HIV negative individuals is associated with a higher risk of HIV infection – this heightened risk is primarily attributed to engaging in high-risk sexual behaviour, potential exposure to violence, and the sharing or re-use of needles (Hammer et al., 2018; Hatcher et al., 2022; Jaguga et al., 2022; Kuteesa et al., 2019; UNAIDS, 2020, 2022c). Alcohol heavy episodic drinking is elaborated further below.

Notably, Sub-Saharan Africa is reported to have the highest global prevalence estimate of Heavy Episodic Drinking (HED – often known as alcohol binge drinking) with over half of drinkers (50.2%) in the region participating in HED, compared to the global average of 39.5% drinkers (Hammer et al., 2018; Sileo et al., 2020). The WHO defines HED as consuming at least 60 grams of pure alcohol on at least one occasion in the past 30 days (Hammer et al., 2018). HED is associated with a higher risk of developing chronic diseases such as liver cirrhosis, certain cancers (e.g., liver, breast, larynx, colon and oesophagus), and cardiovascular diseases(Hammer et al., 2018). It also exacerbates mental health issues, including depression and anxiety, and increases the risk of engaging in risky and violent behaviours leading to injury, death, or suicide (Hammer et al., 2018). HED can lead to alcohol dependence and addiction, resulting in Alcohol Use Disorder (AUD defined in section 1.1.1.2), creating a cycle of behaviour that can be challenging to break without intervention (Hammer et al., 2018).

According to the 2022 UNAIDS Fact Sheet, HIV negative individuals who inject drugs face a 35 times higher risk of acquiring HIV than individuals who do not use injectable drugs

(UNAIDS, 2022c). In addition, people who inject drugs are reported to account for 3% of all new HIV infections in the Eastern and Southern Africa region (UNAIDS, 2022d). For the Eastern and Southern Africa regions who already have a high prevalence of HIV, injectable drug use becomes an important source of new HIV infections that needs to be specifically targeted with interventions (such as needle and syringe sharing programs). HIV testing services needs to account for individuals who inject drugs and tailor programmes to reach this demographic, as their health needs would differ from non-injectable-drug users.

Further, substance use in HIV positive individuals is associated with poor treatment adherence and increased morbidity and mortality as suggested by a substantiative body of evidence in the literature (Bositis & St. Louis, 2019; Carrasco et al., 2015; Hammer et al., 2018; Hinkin et al., 2004; Jaguga et al., 2022; Khazalwa et al., 2022; Lucas, 2011; Magidson et al., 2020; Mdodo et al., 2015; Paschen-Wolff et al., 2019; Regenauer et al., 2020; Stitzer et al., 2017; UNAIDS, 2020; Velloza et al., 2020). A recent systematic review in 2019 confirmed that in 13 out of 18 studies reviewed, higher Anti-Retroviral Therapy (ART) adherence rates were associated with higher levels of viral suppression (Altice et al., 2019). Thus, any factors compromising treatment adherence would lead to viral non-suppression. Individuals who used alcohol have been reported in a 2020 systematic review to have twice the odds of ART non-adherence compared with those who do not use alcohol (Velloza et al., 2020). A secondary separate analysis by the same authors found that alcohol usage was also reported to double the odds of viral non-suppression in PLWHA (Velloza et al., 2020). Alcohol can also compromise the immune response in PLWHA, leading to an increased biological susceptibility to infections and illness as well as worsening disease progression (Hammer et al., 2018). PLWHA have been found to be at a higher risk of using and abusing substances (alcohol, tobacco and drugs) than the general populace (Duko et al., 2019; Needle et al., 2006). It is reported they use substances to cope with emotional distress, psychiatric illness (Mdodo et al., 2015; Miles et al., 2019) and various socioeconomic problems such as financial stress and unemployment (Paschen-Wolff et al., 2019).

PLWHA are cited to have a two to four times higher likelihood of alcohol usage than the general population, placing them at a higher risk of alcohol binge drinking (Duko et al., 2019). A recent study in South Africa found that about one-third of participants who presented for ART measured positive for ‘unhealthy alcohol usage' (Magidson et al., 2019). The authors defined ‘unhealthy alcohol usage’ by measuring it using a biomarker metabolite which is only formed in the presence of alcohol – phosphatidylethanol (PEth) – which if PEth

> 50ng/mL indicated unhealthy alcohol usage levels (Magidson et al., 2019). In South Africa, HIV prevalence amongst high-risk drinkers is estimated to be 17.0% (95% CI: 14.0-20.5), and amongst recreational drug users is estimated to be 19.2% (95% CI: 15.7-23.2) (Simbayi et al., 2019).

Tobacco smoking is also highly prevalent among PLWHA and is cited to be between 40% - 70% (Miles et al., 2019). Alcohol HED, drug use and tobacco smoking are found to be strongly associated with each other in PLWHA and often occur concomitantly (Hammer et al., 2018; Mdodo et al., 2015; Miles et al., 2019). Smoking in PLWHA contributes to a large amount of excess mortality and morbidity (Miles et al., 2019) and alcohol has been shown to elevate sexual risk through multiple pathways (Kalichman et a l., 2007; Rehm et al., 2017; Scott-Sheldon et al., 2017) and worsen the disease course of HIV/AIDS (Ferreira-Borges et al., 2016; Rehm et al., 2017; Scott-Sheldon et al., 2017; Shuper et al., 2010). Tobacco smoking is a well-known risk factor for many cancers and PLWHA are already known to have elevated risk levels of developing AIDS-defining cancers (e.g. Karposi's sarcoma) as well as non-AIDS-defining cancers (e.g. liver, lung and colon cancer) (Jaguga et al., 2022; Shepherd et al., 2019; Yuan et al., 2022)  PLWHA who smoke thus have a compounded higher risk of developing cancers –  with studies showing that PLWHA who smoke have up to eight times higher risk of developing lung cancer, even after cessation, compared to those who have never smoked (Miles et al., 2019; Shepherd et al., 2019).

### *1.1.1 Key Definitions*

#### 1.1.1.1 Substance Use

Substance Use, as defined by the CDC and WHO, is the use of alcohol, tobacco products, illicit drugs, inhalants and other substances that can be inhaled, injected, consumed or otherwise absorbed into the body with a possible risk of dependence and other negative health effects (CDC National Center for Health Statistics, 2024; World Health Organisation, 2024)

#### 1.1.1.2 Substance Use Disorder (SUD)

SUD in the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) is characterized by a problematic pattern of using one or more substances that leads to significant impairment or distress (American Psychiatric Association, 2013). Substance Use Disorders can involve illicit drugs, prescription drugs, or alcohol. The diagnosis is based on a set of criteria that reflect the consequences of substance use and compulsive behaviours related to it. The DSM-5 categorizes Substance Use Disorders into three levels of severity, based on the number of criteria met by an individual: mild (2-3 criteria), moderate (4-5 criteria), and severe (6 or more criteria). The specific diagnostic criteria can be found in the DSM-V. (American Psychiatric Association, 2013)

#### 1.1.1.3 Alcohol Use Disorder (AUD)

AUD in the DSM-5, is defined as a problematic pattern of alcohol use leading to clinically significant impairment or distress as manifested by at least two of the diagnostic criteria, occurring within a 12-month period (American Psychiatric Association, 2013). The presence of 2-3 criteria symptoms indicates a mild disorder, 4-5 symptoms indicate a moderate disorder, and 6 or more symptoms indicate a severe disorder. The specific diagnostic criteria can be found in the DSM-V. (American Psychiatric Association, 2013)

## 1.2 Literature Review

Systematic reviews and meta-analyses were prioritized as the highest quality of evidence and were given preference in this chapter. If no suitable systematic review was available for the sub-section, then the following evidence was searched for and presented with preference for the highest quality to lowest: randomized control trials (RCTs), then cohort studies, case-control studies and cross-sectional studies. These individual relevant studies were compared in sample size and methodology to demonstrate the quality of data available in the field.

PUBMED, Google Scholar, PLOS ONE, Elsevier, Cochrane, EMBASE and BMJ Open were extensively searched for studies examining substance use in Africa. A number of key themes emerged from the literature review:

1. PLWHA have an increased prevalence of alcohol binge drinking and tobacco use
2. The Risk Factors associated with Substance Use
3. Positive associations between Substance Use, HIV, and Intimate Partner Violence
4. Substance Use and ART non-adherence
5. Gender-Specific Substance Use and HIV Risks

### *1.2.1 Substance Use and HIV in Sub-Saharan Africa*

#### 1.2.1.1 Alcohol, Illicit Drug Use, and HIV in SSA

Two comprehensive systematic reviews are presented below, and their findings compared. The first is by Kuteesa *et al* (2019) and the second by Velloza *et al* (2020). The prevalence and correlates of alcohol binge drinking and illicit drug use, and their association with HIV prevalence or incidence, has been systematically reviewed by Kuteesa *et al* (2019) for the SSA region in several high-risk occupational groups such as: sex workers, truckers, fish workers, uniformed personnel, miners and motor-cycle taxi riders (Kuteesa et al., 2019). Kuteesa *et al* (2019) found 71 eligible research studies published between 1983 and 2017 in 23 different Sub-Saharan African countries including: Kenya, Uganda, Ethiopia, Nigeria, South Africa, Angola, Ghana and Mozambique. Most of the research was conducted in Kenya with a total of 15 studies. South Africa contributed four eligible studies. 60% (n=36) of these studies were published between 2014 and 2017 demonstrating a marked increase in interest/funding in HIV and substance use in SSA research in recent years. Alcohol use was focused on heavily as 35 of the papers reported on it alone, with the most researched high-risk occupational group being sex workers (n=42) and then uniformed personnel (n=14).

Velloza *et al* (2020) contributed a systematic review on ART non-adherence amongst PLWHA and alcohol use in SSA. Velloza *et al*'s (2020) systematic review of 56 articles focused solely on alcohol use as the only substance and included the general adult (18+)

population, not specific occupational groups, with a mix of male and female participants. Velloza *et al*'s (2020) search strategy included publications between 1990 and 2019, with majority (30%) of their eligible studies coming from South Africa (n=17 studies out of a total of 56), and three studies (5%) coming from Kenya.

Kuteesa *et al* (2019) reported the pooled prevalence estimate of alcohol binge drinking in SSA, among the high-risk occupational groups, as 35.7% (95% CI: 24.2%, 47.2%). Velloza *et al* (2020) reported a pooled prevalence estimate of alcohol binge drinking in the general SSA adult population as 23% (Velloza et al., 2020). This is much lower than what Kuteesa *et al* (2019) found and is expected as Kuteesa *et al* (2019) targeted high-risk occupational groups. Velloza *et al* (2020) found that the overall prevalence of non-adherence to ART amongst those who binge drank alcohol was 34%, compared to 18% amongst those who did not use alcohol. Those who binge drank had twice the odds of treatment non-adherence (pooled odds ratio: 2.3; 95% CI: 1.9-2.7; $p<0.001$), and twice the odds of viral non-suppression (pooled odds ratio: 2.47; 95% CI: 1.58-3.87; $p<0.001$) than those who did not use alcohol (Velloza et al., 2020).

Kuteesa *et al* (2019) also found that a positive association was found in the majority of studies that reported on the association between HIV and alcohol binge drinking. HIV and binge drinking was found to be associated with factors such as: age, intimate partner violence, drug use, number of traumatic events, being involved in violence or combat, recruiting clients from clubs/bars, and reporting rape as their first sexual act. Due to the high heterogeneity of the illicit drug use studies the authors did not report a pooled prevalence estimate. The drug substances most frequently reported on in all of the studies Kuteesa *et al* (2019) reviewed were marijuana, khat and injectable drugs. The factors associated with illicit drug use and HIV were found to be: having a low level of completed education, post-traumatic stress disorder, being single, being younger at sexual debut and having a larger number of clients (if sex worker). Drug use and binge drinking was shown to have a consistent positive association with intimate partner violence (Kuteesa et al., 2019).

Alcohol Use Disorder (AUD) in SSA in the general adult population was systematically reviewed by Gelle *et al* (2024). Adult men and women from East, West and Southern Africa were represented in Gelle *et al*'s (2024) review, with Central Africa not being represented due to their being no eligible studies on AUD. Gelle *et al* (2024) found a total of 16 eligible publications on AUD and stated that their search timeframe included up until June 2022 –

with no earlier cut off point explicitly stated in their methodology. The earliest paper included in their review was published in 2006. Five of their studies were from Ethiopia, two from Kenya, two from Nigeria, one from Tanzania, one from South Sudan and three from South Africa (Gellé et al., 2024). Gelle *et al* (2024) reported the prevalence of AUD in South Africa to range between 1.2% to 26.5%, and the prevalence of AUD in Kenya to be 31.7% (Gellé *et al*., 2024).

#### 1.2.1.2 Tobacco Use and HIV in SSA

Murphy, Liu and Parascandola (2019) took Demographic Health Surveys (DHS) and AIDS Indicator Surveys (AIS) from 25 sub-Saharan African countries and analysed the association between cigarette smoking and HIV status, as well as the relationship between smokeless tobacco use and HIV status. The DHS and AIS included nationally representative samples of both men and women between the ages of 15 and 59 years (n=286 850) (Murphy et al., 2019). Murphy, Liu and Parascandola (2019) analysed DHS and AIS data from the following SSA countries: Mali, Niger, Gambia, Senegal, Sierra Leone, Liberia, Cote d'Ivoire, Gabon, Ghana, Togo, Burkina Faso, Cameroon, Uganda, Ethiopia, Kenya, D.R. Congo, Zambia, Zimbabwe, Malawi, Lesotho, Swaziland and Namibia. Of notable absence is South Africa.

Murphy, Liu and Parascandola (2019) reported that the prevalence of smokers in Kenya was 8.63% and did not report anything for South Africa. As stated above their dataset did not include South Africa. Murphy, Liu and Parascandola (2019) found the overall prevalence for cigarette smoking in SSA was 8.28% and for smokeless tobacco was 1.89%, with prevalence generally skewed towards the 50 years and older age group, being male, having a lower attainment of education level, manual and agricultural workers, and poorer wealth indices. Murphy, Liu and Parascandola (2019) reported that PLWHA had a higher smoking prevalence (10.63%) than those who were HIV negative (8.14%), and that PLWHA had a significantly higher odds of smoking cigarettes and using smokeless tobacco than HIV negative individuals with or without adjustment for confounders. In addition, they found that those who were more sexually active or who had multiple partners were significantly more likely to smoke than those who have never had sex before. Upon comparative country analysis, Murphy, Liu and Parascandola (2019) found that the prevalence of cigarette

smoking and smokeless tobacco use varied widely across countries, as did HIV prevalence, and the trends of socioeconomic factors associated with smoking and smokeless tobacco.

#### 1.2.1.3 Historical systematic reviews of relevance for HIV and Substance Use in SSA

It is worthwhile to note older systematic reviews that were conducted by Pithey and Parry (2009) and Fisher *et al* (2007) looking at the association between alcohol use and HIV in SSA studies in the general population. These studies found a positive association between the frequency and quantity of alcohol and HIV prevalence (Fisher et al., 2007; Pithey & Parry, 2009). This older systematic review demonstrates that the association between HIV and alcohol use is well-known in the literature.

A systematic review by Reid in 2009 looked at injection drug users (IDU) and HIV in Africa. Reid (2009) reported that the most injected drug in Africa was heroin, followed by cocaine and speedball (heroin and cocaine combined). Reid (2009) reported the HIV prevalence amongst IDU in South Africa to be 20%, and 36% in Kenya. Reid (2009) also reported that amongst IDU in Kenya needle sharing rates varied from 27-81% (ever) to 28-52% (in the past 6 months), and in South Africa 56-86% (in the past 30 days) (Reid, 2009). This older study highlights the important need for an updated systematic review, and – due to the high HIV prevalence amongst IDU – the urgent need for specialised and targeted HIV treatment and testing that caters to this high-risk demographic. The integrated HIV care approach should include needle and syringe sharing programs to reduce the incidence rate of HIV amongst IDU.

### *1.2.2 Substance Use and HIV in Kenya*

A systematic review done in 2022 assessed substance use disorder research published between 1982 and 2020 in Kenya and found cross-sectional epidemiological studies (n=129) that covered the general population, adults and adolescents (n= 39), individuals with non-communicable diseases, primary and secondary school students, individuals who used injectable drugs (n=11), general patients, men who had sex with men, university and college students, sex workers, psychiatric patients, vulnerable youth and orphans, PLWHA (n=6), healthcare workers, criminals, military, teachers and pregnant women (Jaguga et al., 2022).

Majority of these studies assessed alcohol use (n=109) and tobacco use (n=80), with fewer studies assessing khat (n=34), opioids (n=21), sedatives (n=19), cocaine (n=19), inhalants (n=16), cannabis (n=14), hallucinogenic substances (n=7), prescriptions medications (n=4), newer drugs on the market (n=1) and ecstasy (n=1) (Jaguga et al., 2022).

#### 1.2.2.1 Alcohol Use and HIV in Kenya

From the 109 papers on alcohol use in Kenya that Jaguga *et al*. reviewed, they found that the 12-month prevalence rate for hazardous alcohol use ranged from 2.9% among general adults in the community to 64.6% in the female sex workers group. The prevalence of alcohol dependence ranged from 8% in the female sex workers living with HIV, to 33% among men who had sex men who were commercial sex workers. Of import to my study are the socio-demographic factors Jaguga *et al*. (2022) found to be associated with alcohol use, including being male, unemployed, self-employed, having a lower socio-economic status, being single or separated from one's romantic partner, living in a larger household, having a family member struggling with an alcohol use problem, and having alcohol brewed locally in the home. Alcohol was also found to be associated with various negative health outcomes such cardiovascular issues, glucose intolerance, defaulting from tuberculosis treatment, diabetes mellitus, depression, intimate partner violence, tobacco use, risk of oesophageal cancer, risk of being involved in road traffic accidents, risk of having injuries and risk of suicidal behaviour (Jaguga et al., 2022).

#### 1.2.2.2 Tobacco Use and HIV in Kenya

Jaguga *et al*. reported the lifetime prevalence of tobacco use to be from 23.5% in healthcare workers to 84.3% in psychiatric patients. There were only two socio-demographic factors associated with tobacco use: being male and living in an urban area. However, there were several negative health factors linked to tobacco use: hypertension, oral leukoplakia, pneumonia, increase risk of laryngeal cancer, ischemic stroke, diabetes mellitus, injury risk in the past 12 months, emotional abuse, and psychological intimate partner violence (Jaguga et al., 2022).

#### 1.2.2.3 Illicit Drug Use and HIV in Kenya

Jaguga *et al.* (2022) reports further on the socio-demographic factors that were found to be associated with khat, cannabis, opioid, cocaine, and other substances were: being male, unemployment, comorbid tobacco and alcohol use, younger age (less than 35), higher level of income, childhood exposure to physical abuse, depression, risky sexual behavior, hepatitus-C virus infection and HIV-HCV co-infection (Jaguga et al., 2022). Khat seemed to be the most well researched substance other than tobacco and alcohol in Kenyan literature.

Phyllys *et al* (2022) – published after Jaguga *et al.*'s (2022) systematic review - studied substance usage in a group of 224 sex workers in Mombasa County, Kenya. They conducted a cross-sectional study to determine the prevalence of drug use among both male and female adult sex workers coming to a local health service centre. 92% of their sample was aged between 18 and 35, and 78% were women. 99% tested positive for at least one drug, with 68% using alcohol, 63% using cotinine (metabolite of nicotine), 28% on opioids (heroin), 17% had tetrahydrocannabinols (THC – psychoactive part of marijuana), 16% on amphetamines (khat), 8.2% on cocaine and 7.7% on benzodiazepines. 2.02% of participants used only one drug, 5.5% of their participants used two drugs simultaneously, 9.23% used three drugs, 16% four drugs, 31% used five drugs, 34% six drugs, and 1.52% used seven drugs (Phyllys et al., 2022). The authors reported that alcohol, cotinine, opioids, and THC were the most common multi-drug combination. They found that cotinine and opioids were used more by the younger age group of 18-35 versus the older age groups above 35 years. Phyllys *et al* (2022) found that cocaine and benzodiazepine usage was higher for those sex workers in formal employment versus those who were unemployed or informally employed. Their study highlights that drug users often use a combination of more than one drug simultaneously – thus any intervention for HIV and substance use must consider multiple drugs and not be isolated to one type of drug. The study's sample size was quite small and heavily weighted towards women. The study could have been strengthened with a bigger sample and a more gender balanced sample to increase generalizability.

### *1.2.3 Substance Use and HIV in South Africa*

A PubMed and Cochrane search for systematic reviews on substance use/alcohol use/tobacco use/IDU and HIV in South Africa published in the last five years returned no results. Systematic review results were generalized to SSA or the Africa region in general, but none for South Africa specifically. A literature search in PUBMED, Google Scholar, PLOS ONE, Elsevier, EMBASE and BMJ Open produced a great variety and depth of studies for South Africa, however this section will focus on several key studies published in the last five years.

#### 1.2.3.1 Alcohol Use and HIV in SA

Hatcher *et al* (2022) studied intimate partner violence (IPV), alcohol misuse and HIV risk behaviours in 2454 adult heterosexual men in an informal, peri-urban settlement in Johannesburg, South Africa (SA). The men in their study were between 18 and 40 years of age. Their study used the syndemic theory as their framework for analysis, which posits that the cluster of alcohol abuse, IPV and risky sexual behaviours have a synergistic effect on heterosexual men's HIV risk (Hatcher et al., 2022). The authors included the covariates of: education, age, relationship status, employment, housing type (formal, informal), food security and migrancy working. In their regression models they controlled for age, education, and relationship status and adjusted for clustering. 71,6% reported having one or more types of risky behaviours where problem drinking, inequitable gender views and perpetration of IPV occurred simultaneously (Hatcher et al., 2022). Problematic drinking on its own was found to significantly increase the odds of high-risk sexual behaviour by 1.6 (aOR 1.60, 95% CI (10.5-2.45). Problematic drinking combined with one other risk behaviour increased the odds of high-risk sex by five times (Hatcher et al., 2022). Those who reported having all three of the risky behaviours (problem drinking, inequitable gender views and IPV) had 12 times greater odds of high-risk sexual activity (aOR 12.56, 95%CI 3.92-40.22) (Hatcher et al., 2022). This study was robust in its sample size, and methodology with the syndemic theory underpinning their analysis. They only sampled men from a peri-urban area, thus their findings cannot be completely generalizable to heterosexual men in urban or rural settings.

HIV and alcohol use was studied in 33 HIV-positive pregnant women in Cape Town, SA(Washio et al., 2021). The women were between the ages of 18 and 45, with the average

participant being 32 (SD 5.7) and they were enrolled into an alcohol reduction and ART adherence intervention. 55% of the women in the study reported alcohol use in the past month, and urine screening revealed that the women used methamphetamine, mandrax (methaqualone) and marijuana. 27% reported a history of IPV, with 12% reporting a history of sexual abuse (Washio et al., 2021). Their study lost many participants in their follow up period, with their final sample only having five pregnant women. The final sample showed a 20% improvement in ART adherence and reduced alcohol intake – where all five women were previously at risk for AUD at baseline, but at follow-up only two women were at risk of an AUD (Washio et al., 2021). This study had a very small sample size, thus the results are not generalizable and the statistical power of their outcomes are low, however it is still important to include this paper to demonstrate a need for higher quality research in alcohol use and HIV in SA.

HIV-negative pregnant women, sexual risk and alcohol use was studied by Miller *et al* (2023) in Cape Town, SA. They had a sample size of n=1201, with an average age of 26.6 years (SD 5.9). Their study found that women who reported alcohol use vs. those who did not drink were generally younger in age, less likely to live in informal housing, had a higher risk of IPV, often reported that they did not want the baby and that they felt the timing of the baby was bad, they were more likely to have multiple partners, they were less likely to live with their primary partner, and those partners often had unknown HIV statuses (Miller et al., 2023). This study focused on pregnant women, making its results only relevant to this demographic.

AUD in SSA in the general adult population was systematically reviewed by Gelle *et al* (2024) – cited and described above in section 1.2.1.1. Gelle *et al* (2024) reported the prevalence of AUD in South Africa to range between 1.2% to 26.5%. This wide range of prevalence reported is due to different assessment tools that were used in the AUD publications, making comparison and standardisation difficult (Gellé et al., 2024).

#### 1.2.3.2 Tobacco Use and HIV in SA

Stanton *et al* (2021) examined how smoking impacts depression and HIV medication adherence in a sample of 289 adult men and women in peri-urban Cape Town, South Africa. The average age of their sample was 31.1 years old (SD = 8.3). They found that the

prevalence of regular tobacco smoking to be 24% and that this regular use of tobacco was associated with decreased cognitive functioning in both men and women (Stanton et al., 2021). 'Regular tobacco' use was defined as daily, almost daily or weekly usage. They found that most of the participants had a major depressive disorder (MDD), with the average depression severity score for the sample being 33.1 (SD=13.5, mild MDD cut-off is 20) (Stanton et al., 2021). The authors further investigated the link between AUD and tobacco use severity and found a significant positive correlation between the two ($r(273) = 0.35$, $p<0.01$).

#### 1.2.3.3 Illicit Drug Use and HIV in SA

A detailed cross-sectional survey by Scheibe *et al* (2020) examined the prevalence of hepatitis B (HBC), hepatitis C (HCV) and HIV amongst people who use drugs (including those who inject drugs), sex workers and men who have sex with men. They conducted this survey in South Africa across seven different cities: Cape Town, Durban, Pietermaritzburg, Mthatha, Port Elizabeth, Johannesburg and Pretoria. Their total study sample size was n=3439, of which 1528 were sex workers (44%), 746 were men who have sex with men (22%) (MSM), and 1165 were people who use and/or inject drugs (34%) (PWUD/ID) (Scheibe et al., 2020). The average age of a participant was 29 (IQR 25-35), however in Cape Town PWUD/ID were generally older with only 8% under 25 years of age.

HIV prevalence was found to be 37% amongst this study sample (with the highest rates amongst sex workers (47%)), HBV prevalence was 4%, and HCV prevalence was 16% (with the highest rates amongst people who use drugs (PWUD)) (Scheibe et al., 2020). The prevalence of HIV in PWUD was 19%, and in MSM was 43% (Scheibe et al., 2020). However, only 51% of PWUD/ID who were HIV positive were accessing ART. There are no reliable estimates for the population size of PWUD/ID in South Africa, as non-regulated and illicit drugs would be underreported or not reported, but modelling estimates approximate between 67000 and 75000 people (Scheibe et al., 2020). In Scheibe *et al*'s (2020) study 28% of the total sample reported injecting a drug in the prior month, but amongst the PWUD/ID about 80% reported using injectable drugs. Amongst MSM injectable drug use was 3% in Pretoria and Johannesburg, and 9% in Cape Town. No sex workers reported using injectable drugs in the last month as they preferred to smoke or inhale heroin (Scheibe et al., 2020).

85% of all PWUD/ID in the study sample were male, and majority were disproportionally homeless with 57% homelessness in Cape Town to 70% in Durban. Almost all (82%) of the n=3439 participants reported having used at least one substance in the prior month, with alcohol being the most commonly reported (46%). Heroin (locally called nyaope or whoonga) was the most reported used drug in the prior month, with 33% of the total 3439 sample reporting usage. Methamphetamine followed heroin with 14% reported usage, then cannabis at 13%, cocaine 6%, and methcathinone 2% (Scheibe et al., 2020). Results also show a preference of MSM for methamphetamine and PWUD/ID for heroin (Scheibe et al., 2020).

PWUD/ID were the least sexually active (in the last month) amongst the three population groups studied – ranging between 29% and 55% depending on the city. In comparison, 69% of MSM and 98% of sex workers reported sexual activity in the prior month. 38% of all participants reported using substances at the last sexual event, with 53-73% of sex workers reporting mostly alcohol usage. 1-35% of PWUD/ID, and 22-35% of MSM reported substance use at last sexual event but did not report a preference like sex workers for alcohol (Scheibe et al., 2020).

### *1.2.4 Substance Use, HIV and Gender*

Policies and studies on substance use need to be customized according to gender, recognizing the distinct patterns of consumption and sexual risk behaviours between men and women.

#### 1.2.4.1 Alcohol Use, HIV and Gender

The link between alcohol and increased HIV and STI risks is clearly established, driven by unsafe sexual practices, including unprotected sex, coercive sex, engagements with multiple partners, sexual assault, and sex in exchange for goods or money (Hammer et al., 2018). Such risks are often imposed on women due to their male partners' heavy or irresponsible alcohol use (Hammer et al., 2018). Moreover, the presence of untreated STIs can boost the odds of HIV transmission, thus alcohol magnifies the risk of HIV infection for women through the indirect pathways related to their male partners' drinking (Hammer et al., 2018). The habitual drinking of alcohol during sexual encounters is also associated with a rise in male-perpetrated

sexual aggression, inequitable gender views and IPV (Hammer et al., 2018; Hatcher et al., 2022).

Men's alcohol-related risks are predominantly due to binge drinking habits that lead to dangerous or aggressive behaviour and IPV (Ferreira-Borges et al., 2016; Hatcher et al., 2022; Kalichman et al., 2007; Magidson et al., 2019). On the other hand, women's alcohol-related risks are often influenced by their male partners' drinking patterns (Ferreira-Borges et al., 2016; Kalichman et al., 2007; Magidson et al., 2019). According to the WHO Global Status Report on Alcohol and Health (2018), there are 237 million men and 46 million women suffering from alcohol use disorders (AUDs), highlighting a significant gender disparity (Hammer et al., 2018).

Hatcher *et al* (2022) found in their univariate logistic regression models on heterosexual men, alcohol abuse, IPV and HIV risk – cited above in section 1.2.3.1 – that men who completed high school education level, and who reporting having a partner but living apart, had lower odds of high risk sexual behaviour. Age, migrancy working and living in informal housing types were found to be associated with risky sexual behavioursin heterosexual men (Hatcher et al., 2022).

#### 1.2.4.2 Tobacco Use, HIV and Gender

Murphy, Liu and Parascandola (2019) found that across 25 SSA countries' DHS and AIS national surveys (n= 286 850), women had a higher HIV positive prevalence (6.95%) than men (4.75%). In addition, they found that cigarette smoking was far more prevalent in men (16.55%) than in women (0.76%). This is supported by Stanton *et al* (2021) who found that the prevalence of habitual tobacco smoking amongst men was 48.1%, which was much higher than 15.5% amongst women, although their sample size was small n=289 (Stanton et al., 2021). Miles *et al* (2019) who amongst a larger study sample size of n=1607 PLWHA, found that the prevalence of current smoking amongst men to be 46.6%, which was marginally higher than amongst women 46.0%. The two papers had a similar finding amongst men, but large differences in the prevalence of smoking amongst women. This may be due to the different study designs as Stanton *et al* (2021) recruited all of their participants from the same longitudinal cohort who may have been matched/paired, whereas Miles *et al* (2019) sampled from individuals waiting at a clinic for treatment ensuring a slightly more random

sampling process than Stanton *et al* (2021). Stanton *et al* (2021) also reported that men's tobacco addiction risk was 8.5 times greater than women's (B=8.50, p <0.001, 95% CI: 5.81-11.19). This may be correlated to the study find of Stanton *et al's* (2021) where habitual tobacco smoking was strongly positively associated with the ability to function without pain but only in men, whereas in women the relationship was found to be not significant (Stanton et al., 2021). The authors discuss that this is possibly due to the gendered dynamics of pain-coping strategies in PLWHA: men preferring to use substances and distraction, and the women preferring social support and positive emotion-based approaches (Stanton et al., 2021).

Of interest is an older study done by Peltzer (2011) looking at the associated factors of smoking initiation in male and female adolescents in seven African countries. Peltzer (2011) found that early tobacco smoking initiation amongst males was associated with reporting having ever used drugs, having ever been drunk from alcohol, and having ever had sex. Amongst females it was associated with higher education, having ever been drunk from alcohol, being exposed to parental or guardian tobacco usage, and suicidal ideation (Peltzer, 2011).

#### 1.2.4.3 Illicit Drug Use, HIV and Gender

Three studies in Kenya found that the drivers for injectable drug use amongst women included intimate partner influences, unexpected pregnancy stresses, gender inequalities, social suffering, as well as perceived possible contraception usage as it causes amenorrhea (Jaguga et al., 2022). A paper that Jaguga *et al* (2022) included, but that deserves highlighting is Mburu, Limmer and Holland (2019), who did a secondary data analysis on qualitative data of 24 interviews and three focus group discussions with 45 women who injected drugs, and five interviews with key stakeholders. They found that unsafe conditions arising around the injecting of drugs and unprotected sex was due to a 'high-risk environment' that the women were involuntarily experiencing (often at the hands of their partners or clients). Unsafe injecting of drugs occurred in the form of sharing needles and injecting drugs during sex, a low-risk perception of their HIV risk, inequitable gender power imbalances between parties, poor availability of needles and condoms, and economic pressures the women were facing (Mburu, Limmer and Holland, 2019). Furthermore, our search suggested that there is a

limited amount of studies on specifically the role of sex (male/female), gender and illicit drug use in SSA. There is a large body of research on female sex workers and drugs, however there are few papers on other women who are part of this high-risk occupational group.

## 1.3 Problem Statement

The literature review highlights the complex interplay between different types of substance use and HIV in SSA, underscoring the need for substance-specific targeted interventions that consider the specific needs and risks of different populations, including gender-specific approaches. However, there were a few notable research gaps in the literature:

Kuteesa *et al* (2019), cited above, mentions a few times that many of their studies reported on prevalence and not on the correlates of substance use and HIV. A concerning finding of Kuteesa *et al*'s (2019) paper was that of the 25 papers who did report on association or risk factors between alcohol misuse, drug use and HIV, only half these papers adjusted for confounders in their analysis. Kuteesa *et al* (2019) found that whilst alcohol binge drinking research had validated tools that were used, almost all of the studies that reported on illicit drug use had no validated tools and did not use a clear or consistent reporting timeframe – sometimes 'daily usage', other times 'ever used', or not specified (Kuteesa et al., 2019).

A recent systematic review (done in the last five years) on smoking and HIV in SSA was not found during our search. Murphy, Liu and Parascandola's (2019) paper was valuable as it analysed a large representative sample from 25 SSA countries on smoking and HIV, however it did not have the broad chronological comparative perspective of a systematic review. Most of the studies on the impact of tobacco on different health outcomes for PLWHA are notably concentrated in High Income Countries (HIC) such as the United Sates and Canada, showcasing a need for more research on this topic in Low-to-Middle Income Countries (LMIC) (Stanton et al., 2021).

In addition, no recent systematic review was found on IDU and HIV in Africa published in the last 5 years. Whilst literature on drug users is scarce, what is available focuses on users who inject drugs and not on the broader scope of drug users (Scheibe et al., 2020).

Of interest from Jaguga *et al*.'s research is how few studies have focused on substance use in PLWHA in Kenya – their systematic review only found six cross sectional epidemiologic studies between 1982 and 2020 in Kenya.

Substance use is a known HIV risk factor, and in PLWHA, it can worsen their adherence to ART and overall health outcomes by increasing morbidity and mortality. This study will contribute to a needed (and lacking) body of knowledge on the correlates of substance use and HIV in SSA countries (specifically Kenya and South Africa), and PLWHA and substance use in LMIC (Kuteesa et al., 2019; Scheibe et al., 2020; Stanton et al., 2021; Jaguga et al., 2022). This study's findings can then inform further hypotheses to enhance integrated care and substance use interventions for South African and Kenya PLWHA populations (such as needle sharing programs).

## 1.4 Aim

This study aims to investigate the association between HIV and substance use in South Africa and Kenya using the cross-sectional AWI-Gen population-based study data. This secondary analysis of AWI-Gen data will allow the similarities and differences in HIV profiles and substance use behaviours to be explored across these two sub-Saharan African countries.

# CHAPTER 2

This chapter consists of a description of the methods of the primary study that this study drew its dataset from in section 2.1. The chapter then describes the methods of this secondary study (2.2), detailing the study sites (2.3), study population (2.4), study sampling (2.5), variables of interest (2.6), data management (2.7) and statistical analysis (2.8). The chapter ends with ethical considerations (2.9).

# 2. METHODS

## 2.1 Description of Primary Study

The African Wits-International network for Genomic studies' (AWI-Gen) study was designed as a cross-sectional population study (Gómez-olivé et al., 2017; Ramsay et al., 2016). It was a large-scale genomic and environmental study of body composition and cardio metabolic disease risk (Ramsay et al., 2016) funded by the H3Africa Consortium (Gómez-olivé et al., 2017). The primary study included 10 703 participants between the ages of 40 and 60 years across four African countries: Burkina Faso, Ghana, Kenya and South Africa.

The AWI-Gen study leverages on the already pre-existing Health and Demographic Surveillance System (HDSS) centres and the Developmental Pathways for Health Research Unit (DPHRU) longitudinal cohorts by recruiting part of its sample from these studies. The data that this study has already collected includes demographic, health history, environmental, behavioural, and biomarker data from enrolled adults in these four countries at already established INDEPTH network study sites. The primary AWI-Gen data were collected through questionnaires, anthropometric measurements and collected biospecimens. HIV status was determined by both testing and self-report. Substance use data was collected for tobacco use, alcohol use and drug use. The study has been described in greater detail in previous publications (George et al., 2019; Mohamed et al., 2019; Ramsay et al., 2016; Wagner et al., 2018).

## 2.2 Description of Secondary Study

This study is designed as a secondary cross-sectional data analysis of pre-existing AWI-Gen data focusing on participants living with and without HIV/AIDS and their reported substance use behaviours.

## 2.3 Study Sites

*2.3.1 Primary study:* The Primary AWI-Gen study sites included four rural community research sites in Nanoro (Burkina Faso), Navrongo (Ghana), Agincourt and Dikgale (South Africa); and two urban community research sites in Nairobi (Kenya) and Soweto (South Africa).

*2.3.2 Secondary study:* The South African and Kenyan sites that were of interest for secondary data analysis included two rural community research sites in Agincourt and Dikgale (South Africa); and two urban community research sites in Nairobi (Kenya) and Soweto (South Africa). The Nairobi, Dikgale and Agincourt sites were all HDSS research sites. The Soweto site formed part of the DPHRU (Gómez-olivé et al., 2017). Ghana and Burkina Faso were excluded as they did not have HIV status data recorded.

## 2.4 Study Population

*2.4.1 Primary study:* The primary study included a population of 10 703 participants, between the ages of 40 and 60, drawn from Burkina Faso, Ghana, Kenya and South Africa. An additional 1021 participants over the age of 60 were recruited at the Agincourt centre. All participants were recruited into the study between August 2013 and August 2016 All participants were residents at one of the six sites. Participants were between the ages of 40 and 60 as this age range is the period where cardiometabolic diseases are most likely to present and the original AWI-Gen study focused on cardiometabolic diseases. Some individuals below the age of 40 were accidentally recruited into the primary study and the PI received ethics approval to keep and analyse their data.

Exclusion criteria were: first degree relatives of the participants, pregnant women, individuals with physical impairments preventing blood pressure measurements, and recent immigrants (<10 years) into the communities. There was no selection based on body composition, infection, or disease history.

*2.4.2 Secondary study:* The study population for this secondary data analysis included 7919 men and women participants drawn from Kenya and South Africa. These participants resided in the areas serviced by the local HDSS centres or DPHRU (Gómez-olivé et al., 2017; Ramsay et al., 2016). Participants were all between the ages of 40 and 60 (Ali et al., 2018; Ramsay et al., 2016)(Ali et al., 2018; Ramsay et al., 2016).

## 2.5 Study Sampling

*2.5.1 Primary study:* Participants were identified and selected using random sampling frames already in use at each of the HDSS/DPHRU study sites (Ali et al., 2018)(Ali et al., 2018).

In Nairobi, Kenya, male and female participants were selected randomly using a geographical sample frame that covered the peri-urban districts of Korogocho and Viwandani. (Ali et al., 2018)(Ali et al., 2018)

In Dikgale, South Africa, participants were selected randomly from a regional geographical sampling frame. (Ali et al., 2018)(Ali et al., 2018)

In Agincourt, South Africa, participants were sampled from the 2013 population census by first identifying all adults who were aged 40 and above as of 1 July 2014 and who were permanently residing in the study area. Participants who had been research subjects in previous studies were also invited to participate. The authors used a gender-specific sampling fraction for Agincourt to ensure an equal balance of men and women were recruited, as the area has a bias of more women. (Ali et al., 2018)(Ali et al., 2018)

In Soweto, South Africa, some of the female participants were recruited from the 'birth to 20 plus' cohort study. The male and other female participants were recruited through random selection using a geographical-based sampling frame. (Ali et al., 2018)(Ali et al., 2018)

*2.5.2 Secondary study:* All participants from Kenya and South Africa were included in the sample for this study so no sample size calculation was necessary.

## 2.6 Secondary Data Analysis

Participants with missing data in any of the key variables of substance use and HIV status were dropped from the analysis.

To gain access to the data the data request forms were completed and submitted to the AWI-Gen team for approval. Only questionnaire and interview data were requested for this analysis. No anthropometric or genetic data were requested.

### *2.6.1 Key Variables of Interest*

HIV status was determined as 'Positive' or 'Negative' if the participants self-reported or tested, it was reported as 'Other' if they were not asked, did not want to be tested or there was no data.

Tobacco usage was recorded as 'Never', 'Current', 'Used to' or 'Missing'.

Alcohol usage was recorded as 'Never Drank', 'Current Drinker', 'Former Drinker', 'Missing' or 'Not Applicable'.

Drug usage was measured by asking participants if they currently or had in the past ever used any other drugs and answers were recorded as 'Yes', 'No', 'Missing' and 'Don't Know'.

Substance use was a binary 'Yes'/'No' variable generated from Tobacco usage, Alcohol usage, and Drug usage variables. If the participant had used in the past or were currently using any alcohol, tobacco and/or drugs they were given the Substance use value of 'Yes'. All other participants who had reported 'Never' or 'No' to using all of the three substances were given the value of 'No' for Substance use. [1]

[1] Drug usage data in the primary study did not have current and past usage disaggregated like the alcohol and tobacco data. Thus, to compare drug usage with alcohol and tobacco usage, current and past usage had to be combined into a binary outcome variable. This is further discussed in the limitations section in Chapter 4, section 4.3

## 2.7 Data Management

For secondary data analysis separate working copies of the original data set were saved. This was to maintain the original data set untouched. This also allowed for version control as the working data set was modified, cleaned, and new variables were generated. The data set was kept in an encoded file on the researcher's laptop, which was password and 2-step authentication protected.

## 2.8 Statistical Analysis

The aim of the analysis was to investigate the association between substance use and HIV status in Kenya and South Africa (SA).

The hypothesis was that substance use is positively correlated with HIV status (in both countries), and the factors of education level, employment status, marital status and socioeconomic status effect the odds of using substances.

Potential confounders, as suggested by the literature, were age and sex (see Figure 1).

STATA 14.1 was used to conduct basic summary statistics and the logistic regression models. The Mann-whitney test was used for the continuous variable of age. All other categorical variables were analysed using a chi squared test or/and Fisher's exact tests (for small frequencies).

### *2.8.1 Objective 1*

The first objective was to estimate the prevalence of substance use and the factors associated with substance use in the two SSA countries: South Africa and Kenya.

A binary variable for substance use was generated depending on if a participant indicated that they currently used or had used alcohol, tobacco or drugs. This binary variable was used as the primary outcome variable for Objective 1. Basic descriptive statistics was used to compare demographic data by country, using Chi-square or Fisher's exact tests (for

categorical variables), alongside the Mann-Whitney test (for continuous non-parametric variables), to find any associations. Demographic variables – such as age, sex, educational attainment, employment status, marital status, and economic level – was used to describe the prevalence of substance use in each country and overall.

### *2.8.2 Objective 2*

The study's second objective was to estimate the prevalence of HIV and identify the factors associated with HIV in the two SSA countries.

The same demographic variables were used as in the first objective. HIV status was used as the primary outcome variable for Objective 2. This objective's analysis also looked at individual substance use types: alcohol, tobacco, and drug use, as independent variables. Drug usage data in the primary study was not disaggregated into current and past usage. Thus, to compare drug usage with alcohol and tobacco usage, current and past usage had to be combined. The analysis approach included descriptive statistical analysis by country, categorizing demographic and substance use data by HIV status, and applying Chi-square or Fisher's exact tests to explore associations.

### *2.8.3 Objective 3*

The study's third objective was to examine the association between substance use and HIV infection among participants in the two SSA countries, adjusting for socio-demographic variables that might influence this association.

The analysis involved using the generated binary variable for substance use as the outcome and conducting logistic regressions to examine the relationship. Predictive factors were informed by the literature review and conceptually modelled using a Direct Acyclic Graph (DAG) in Figure 1 to guide the logistic analysis. Included in the DAG, and ultimately the final model were the following variables: HIV status, sex, socioeconomic quintile (SES), highest level of education, marital status, employment/occupational status, and age. Age and

sex were controlled for as confounders, and education, employment, marital status, and socioeconomic status (SES) were included in the model as explanatory variables.

Age was recoded into categorical ranges for the logistic regressions, ’25-49’, ‘50-64’ and ’65 and older’ as used by the KENPHIA and SABSSM V reports to ensure results were comparable (Simbayi et al., 2019; Kenyan Ministry of Health, 2022). The sample used had no participants younger than 25, so a younger category was not coded for.

An overall logistic regression model was run which included both countries, and then separate logistic regression models for Kenya and South Africa.

Due to several participants missing data for their employment status (n= 401) a sensitivity analysis was conducted to determine the bias of missing employment data.

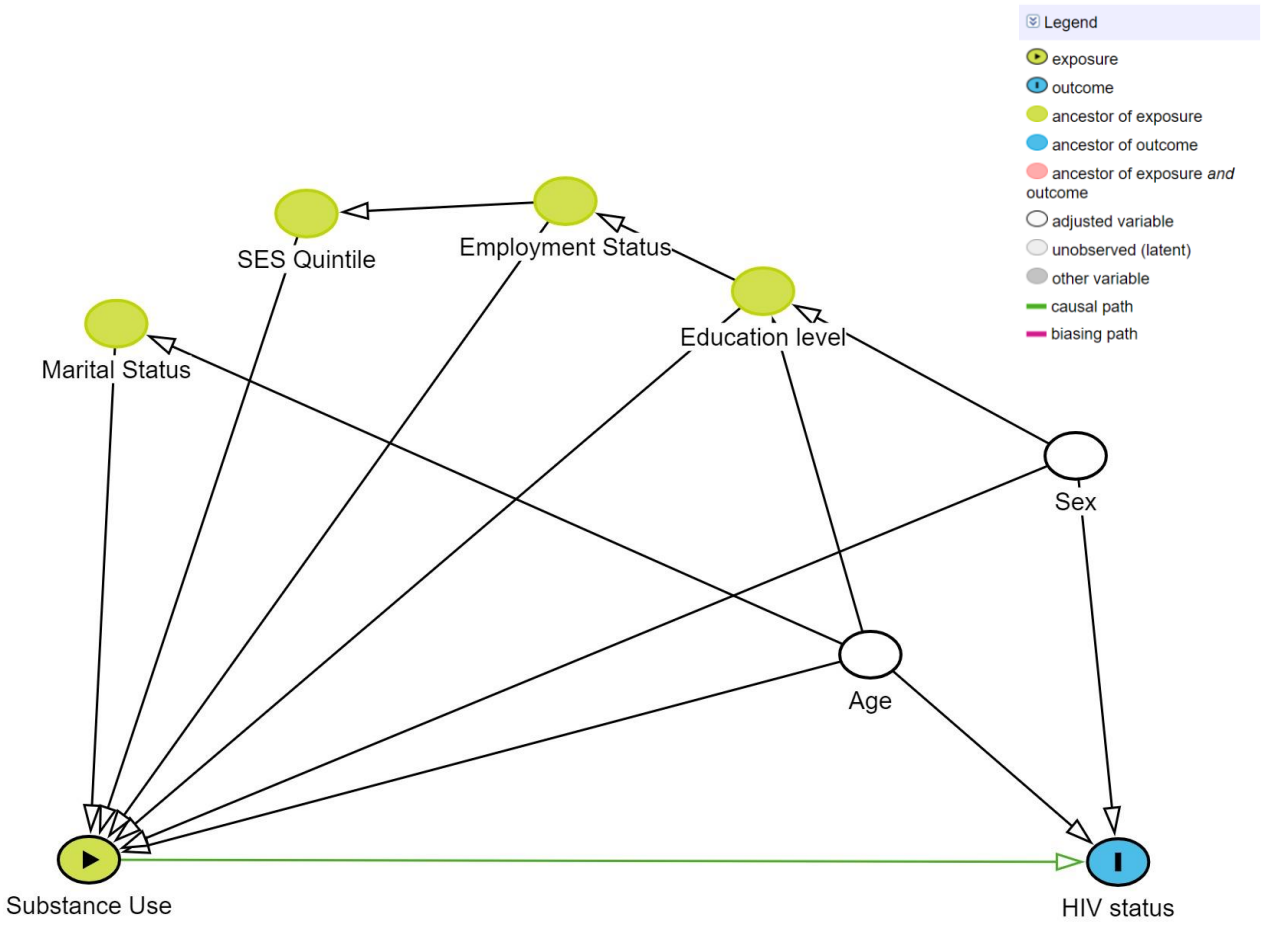


Figure 1: Direct Acyclic Graph (DAG) of the minimal sufficient adjustment sets containing Age & Sex for estimating the total effect of Substance Use on HIV status

## 2.9 Ethical Considerations

The primary study received ethical approval from the Human Research Ethics Committee HREC number M180535, in 2018. This secondary data analysis study received ethical approval, HREC number M210873, in 2021. This study used no living human subjects or animals.

# CHAPTER 3

This chapter presents the results found from the secondary data analysis. It starts with a description of the demographic characteristics of substance users in the study sample in section 3.1, and then of individuals living with HIV/AIDS in the study sample in section 3.2. Prevalence of HIV by substance type found in the dataset is discussed (3.3), before explaining the results of the multivariable logistic regression models (3.4). Three multivariable logistic regression models were done: one for the overall combined sample from both countries (3.4.1), one for the Kenyan data (3.4.2), and one for the South African data (3.4.3). Lastly, this chapter discusses a sensitivity analysis performed on the inclusion and exclusion of one variable due to missing data (3.5).

## 3. RESULTS

### 3.1 Demographic characteristics of substance users

This secondary data analysis originally included 7919 participants across Kenya and South Africa (SA). However, n=1345 (16.98%) respondents did not have information for substance use. Thus, they were dropped from the Table 1 analysis leaving 6574 that were eligible, with 1991 participants in the Kenyan sample and 4583 participants in the South African sample. Of 6574 participants, 52.78% were female (n=3470). Table 1 presents the socio demographic characteristics of the participants stratified by substance use and country. About half of the sample were substance users (54.30%, n=3570); and this stayed consistent even in the Kenyan (51.33%, n=1022) and South African samples (55.60%, n=2548). Across the entire sample the median age of a participant was 52 (IQR: 45-59). In Kenya the median age was 48 (IQR: 44-54), and in SA it was 54 (IQR: 46-61) – reflecting a slightly older sample population in SA. More men than women were substance users in the combined sample (72.30%), Kenyan sample (68.59%) and South African sample (73.78%). In the combined dataset: sex ($p<0.0001$), socioeconomic status (SES) quintile ($p=0.017$), highest level of education completed ($p<0.0001$), marital status ($p<0.0001$), employment status ($p<0.0001$) and HIV status ($p=0.012$) all had a significant association with substance use. Age was not

associated with substance use in the combined dataset, but became significant for Kenya (p=0.015) and South Africa (p=0.0094). Kenya differed from SA and the overall sample in that HIV status was not associated with substance use (p=0.589).

## 3.2 Demographic characteristics of PLWHA

Table 2 presents the demographics characteristics of the participants stratified by HIV status and country. Out of the original sample size 744 (9.40%) respondents did not have information for HIV status and were dropped from this Table 2 analysis, leaving n=7145 for analysis. Overall, 20.94% (n=1496) were HIV positive, and of these PLWHA 59.49% (n=890) were female and had a median age of 49 (IQR: 44-55). In Kenya 13.66% (n=243) of the sample were HIV positive, versus 23.35% (n=1253) in SA. In Kenya and SA, majority of those who were living with HIV were women – 72.02% in Kenya and 57.06% in SA. The following factors were all associated with HIV status in the overall analysis and in the country-specific analyses: SES, marital status, age, highest level of education and employment status.

## 3.3 Prevalence of HIV by substance use type

Table 3 presents three different substance use types according to HIV status and country. Of 6574 participants who had data for both substance use and HIV status 20.09% (n=1321) of them were individuals living with a HIV positive diagnosis. Smoking status, alcohol status and drug use in the combined dataset and individual country datasets were all significantly associated with HIV status. Drug use had the strongest association with HIV status in the combined dataset (p<0.0001). In Kenya alcohol status had the strongest association with HIV status (p=0.002) and in South Africa both alcohol and smoking status had the strongest associations with HIV status (both p<0.0001). Amongst smokers (current and used to), HIV prevalence was 30.89% overall, 22.4% in Kenya, and 32.78% in South Africa. Amongst those who drank alcohol (current and former drinkers) HIV prevalence was 52.91% overall, 49.37% in Kenya, and 53.7% in South Africa. Amongst those who used drugs HIV prevalence was 8.93% overall, 11.62% in Kenya, and 8.33% in South Africa

*Table 1: Demographic characteristics by country, stratified by substance use*

| | **Total** | | p values | **Kenya** | | p values | **South Africa** | | p values |
|---|---|---|---|---|---|---|---|---|---|
| **n** | 6574 | | | 1991 (30.29%) | | | 4583 (69.71%) | | |
| | **Substance users** | **Non- users** | | **Substance users** | **Non-users** | | **Substance users** | **Non-users** | |
| | 3570 (54.30%) | 3004 (45.70%) | | 1022 (51.33%) | 969 (48.67%) | | 2548 (55.60%) | 2035 (44.40%) | |
| **Age (years) (median (IQR))** | 52 (45-59) | 52 (46-59) | 0.7678 | 48 (44-54) | 48 (44-52) | 0.015 | 54 (46-61) | 54 (48-62) | 0.0094 |
| **Sex** | | | <0.0001 | | | <0.0001 | | | <0.0001 |
| women | 989 (27.70%) | 2481 (82.59%) | | 321 (31.41%) | 754 (77.81%) | | 668 (26.22%) | 1727 (84.86%) | |
| men | 2581 (72.30%) | 523 (17.30%) | | 701 (68.59%) | 215 (22.19%) | | 1880 (73.78%) | 308 (15.14%) | |
| **SES (quintile)** | | | 0.017 | | | 0.090 | | | 0.103 |
| missing | 1 (0.03%) | 0 | | 0 | 0 | | 1 (0.04%) | 0 | |
| 1st | 491 (13.75%) | 338 (11.25%) | | 136 (13.31%) | 103 (10.63%) | | 355 (3.93%) | 235 (11.55%) | |
| 2nd | 731 (20.48%) | 672 (22.37%) | | 227 (22.21%) | 224 (23.12%) | | 504 (19.78%) | 448 (22.01%) | |
| 3rd | 569 (15.94%) | 491 (16.34%) | | 229 (22.41%) | 233 (24.05%) | | 340 (13.34%) | 258 (12.68%) | |
| 4th | 783 (21.93%) | 698 (23.24%) | | 190 (18.59%) | 210 (21.67%) | | 593 (23.27%) | 488 (23.98%) | |
| 5th | 995 (27.87%) | 805 (26.80%) | | 240 (23.48%) | 199 (20.54%) | | 755 (29.63%) | 606 (29.78%) | |
| **Highest level of education** | | | <0.0001 | | | 0.035 | | | <0.0001 |
| missing | 2 (0.06%) | 4 (0.13%) | | 0 | 0 | | 2 (0.08%) | 4 (0.20%) | |
| no formal education | 625 (17.51%) | 644 (21.44%) | | 65 (6.36%) | 89 (9.18%) | | 560 (21.98%) | 555 (27.27%) | |
| primary | 1343 (37.62%) | 1305 (43.44%) | | 579 (56.65%) | 564 (58.20%) | | 764 (29.98%) | 741 (36.41%) | |
| secondary | 1433 (40.14%) | 948 (41.56%) | | 362 (35.42%) | 306 (31.58%) | | 1071 (42.03%) | 642 (31.55%) | |

| | | | | | | |
|---|---|---|---|---|---|---|
| tertiary | 167 (4.68%) | 103 (3.43%) | 16 (1.57%) | 10 (1.03%) | 151 (5.93%) | 93 (4.57%) |
| **Marital status** | | <0.0001 | | <0.0001 | | <0.0001 |
| missing | 1 (0.03%) | 1 (0.03%) | 0 | 1 (0.10%) | 1 (0.04%) | 0 |
| married | 1919 (53.75%) | 1559 (51.90%) | 724 (70.84%) | 563 (58.10%) | 1195 (46.90%) | 996 (48.94%) |
| living together | 331 (9.27%) | 148 (4.93%) | 24 (2.35%) | 13 (1.34%) | 307(12.05%) | 135 (6.63%) |
| never married or co-habited | 478 (13.39%) | 288 (9.59%) | 33 (3.23%) | 51 (5.26%) | 445 (17.46%) | 237 (11.65%) |
| divorced with living partner | 336 (9.41%) | 477 (15.88%) | 14 (1.37%) | 31 (3.20%) | 322 (12.64%) | 446 (21.92%) |
| separated with living partner | 204 (5.71%) | 133 (4.43%) | 111 (10.86%) | 106 (10.94%) | 93 (3.65%) | 27 (1.33%) |
| partner deceased | 301 (8.43%) | 398 (13.25%) | 116 (11.35%) | 204 (21.05%) | 185 (7.26%) | 194 (9.53%) |
| **Employment status** | | <0.0001 | | <0.0001 | | <0.0001 |
| missing | 207 (5.80%) | 194 (6.46%) | 3 (0.29%) | 0 | 204 (8.01%) | 194 (9.53%) |
| self employed | 735 (20.59%) | 591 (19.67%) | 422 (41.29%) | 518 (53.46%) | 313 (12.28%) | 73 (3.59%) |
| formal full time | 428 (11.99%) | 309 (10.29%) | 147 (14.38%) | 118 (12.18%) | 281 (11.03%) | 191 (9.39%) |
| part time | 172 (4.82%) | 125 (4.16%) | 24 (2.35%) | 21 (2.17%) | 148 (5.81%) | 104 (5.11%) |
| informal | 677 (18.96%) | 451 (15.01%) | 378 (36.99%) | 243 (25.08%) | 299 (11.73%) | 208 (10.22%) |
| unemployed | 1351 (37.84%) | 1334 (44.41%) | 48 (4.70%) | 69 (7.12%) | 1303 (51.14%) | 1265 (62.16%) |
| **HIV status** | | 0.012 | | 0.589 | | <0.0001 |
| missing | 184 (5.15%) | 111 (3.70%) | 121 (11.84%) | 102 (10.53%) | 63 (2.47%) | 9 (0.44%) |
| positive | 727 (20.36%) | 594 (19.77%) | 126 (12.33%) | 115 (11.87%) | 601 (23.59%) | 479 (23.54%) |
| negative | 2659 (74.48%) | 2299 (76.53%) | 775 (75.83%) | 752 (77.61%) | 1884 (73.94%) | 1547 (76.02%) |

Out of an original sample size of n=7919, 1345 (16.98%) respondents did not have information for substance use

*Table 2: Demographic characteristics by country, stratified by HIV status*

| | **Total** | | p values | **Kenya** | | p values | **South Africa** | | p values |
|---|---|---|---|---|---|---|---|---|---|
| **n** | 7145 | | | 1779 (24.90%) | | | 5366 (75.10%) | | |
| | **HIV+** | **HIV-** | | **HIV+** | **HIV-** | | **HIV+** | **HIV-** | |
| | 1496 (20.94%) | 5649 (79.06%) | | 243 (13.66%) | 1536 (86.34%) | | 1253 (23.35%) | 4113 (76.65%) | |
| **Age (years) (median (IQR))** | 49 (44-55) | 52 (46-59) | <0.0001 | 46 (43-52) | 48 (44-53) | 0.0446 | 50 (44-56) | 54 (47-61) | <0.0001 |
| **Sex** | | | <0.0001 | | | <0.0001 | | | 0.055 |
| women | 890 (59.49%) | 3041 (53.83%) | | 175 (72.02%) | 821 (53.45%) | | 715 (57.06%) | 2220 (53.98) | |
| men | 606 (40.51%) | 2608 (46.17%) | | 68 (27.98%) | 715 (46.55%) | | 538 (42.94%) | 1893 (46.02%) | |
| **SES (quintile)** | | | <0.0001 | | | <0.0001 | | | <0.0001 |
| missing | 7 (0.47%) | 40 (0.71%) | | 0 | 0 | | 7 (0.56%) | 40 (0.97%) | |
| 1st | 212 (14.17%) | 734 (12.99%) | | 38 (15.64%) | 178 (11.59%) | | 174 (13.89%) | 556 (13.52%) | |
| 2nd | 397 (26.54%) | 1180 (20.89%) | | 74 (30.45%) | 318 (20.70%) | | 323 (25.78%) | 862 (20.96%) | |
| 3rd | 231 (15.44%) | 907 (16.06%) | | 51 (20.99%) | 362 (23.57%) | | 180 (14.37%) | 545 (13.25%) | |
| 4th | 332 (22.19%) | 1224 (21.67%) | | 47 (19.34%) | 316 (20.57%) | | 285 (22.75%) | 908 (22.08%) | |
| 5th | 317 (21.19%) | 1564 (27.69%) | | 33 (13.58%) | 362 (23.57%) | | 284 (22.67%) | 1202 (29.22%) | |
| **Highest level of education** | | | 0.035 | | | <0.0001 | | | 0.006 |
| missing | 15 (1.00%) | 64 (1.13%) | | 0 | 0 | | 15 (1.20%) | 64 (1.56%) | |
| no formal education | 273 (18.25%) | 974 (17.24%) | | 13 (5.35%) | 115 (7.49%) | | 260 (20.75%) | 859 (20.88%) | |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| primary | 623 (41.64%) | 2319 (41.05%) | | 174 (71.60) | 860 (55.99%) | 449 (35.83%) | 1459 (35.47%) |
| secondary | 542 (36.23%) | 2025 (35.85%) | | 55 (22.63%) | 537 (34.96%) | 487 (38.87%) | 1488 (36.18%) |
| tertiary | 43 (2.87%) | 267 (4.73%) | | 1 (0.41%) | 24 (1.56%) | 42 (3.35%) | 243 (5.91%) |
| **Marital status** | | | <0.0001 | | | | <0.0001 |
| missing | 36 (2.41%) | 112 (1.98%) | | 0 | 1 (0.07%) | 36 (2.87%) | 111 (2.70%) |
| married | 534 (35.70%) | 3015 (53.37%) | | 108 (44.44%) | 1023 (66.60%) | 426 (34.00%) | 1992 (48.43%) |
| living together | 186 (12.43%) | 372 (6.59%) | | 2 (0.82%) | 34 (2.21%) | 184 (14.68%) | 338 (8.22%) |
| never married or co-habited | 219 (14.64%) | 611 (10.82%) | | 15 (6.17%) | 56 (3.65%) | 204 (16.28%) | 555 (13.49%) |
| divorced with living partner | 247 (16.51%) | 707 (12.52%) | | 9 (3.70%) | 31 (2.02%) | 238 (18.99%) | 676 (16.44%) |
| separated with living partner | 84 (5.61%) | 325 (5.75%) | | 36 (14.81%) | 170 (11.07%) | 48 (3.83%) | 155 (3.77%) |
| partner deceased | 190 (12.70%) | 507 (8.98%) | | 73 (30.04%) | 221 (14.39%) | 117 (9.34%) | 286 (6.95%) |
| **Employment status** | | | <0.0001 | | | | <0.0001 |
| missing | 72 (4.81%) | 330 (5.84%) | | 0 | 2 (0.13%) | 72 (5.75%) | 328 (7.97%) |
| self employed | 200 (13.37%) | 1102 (19.51%) | | 107 (44.03%) | 737 (47.98%) | 93 (7.42%) | 365 (8.87%) |
| formal full time | 202 (13.50%) | 868 (15.37%) | | 21 (8.64%) | 219 (14.26%) | 181 (14.45%) | 649 (15.78%) |
| part time | 90 (6.02%) | 219 (3.88%) | | 4 (1.65%) | 40 (2.60%) | 86 (6.86%) | 179 (4.35%) |
| informal | 217 (14.51%) | 847 (14.99%) | | 95 (39.09%) | 448 (29.17%) | 122 (9.74%) | 399 (9.70%) |
| unemployed | 715 (47.79%) | 2283 (40.41%) | | 16 (6.58%) | 90 (5.86%) | 699 (55.79%) | 2193 (53.32%) |

Out of an original sample size of n=7919, 744 (9.40%) respondents did not have information for HIV status.

*Table 3: Prevalence of HIV by country and by substance use*

| | **Total** | | | p values | **Kenya** | | | p values | **South Africa** | | | p values |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **n** | 6574 | | | | 1991 (30.29%) | | | | 4583 (69.71%) | | | |
| | **HIV+** | **HIV-** | **Missing** | | **HIV+** | **HIV-** | **Missing** | | **HIV+** | **HIV-** | **Missing** | |
| | 1321 (20.09%) | 4958 (75.42%) | 295 (4.49%) | | 241 (12.10%) | 1527 (76.70%) | 223 (11.20%) | | 1080 (23.57%) | 3431 (74.86%) | 72 (1.57%) | |
| **Smoking status** | | | | 0.004 | | | | 0.020 | | | | <0.0001 |
| Never | 913 (69.79%) | 3418 (68.94%) | 174 (58.98%) | | 187 (77.59%) | 1088 (71.25%) | 148 (66.37%) | | 726 (67.22%) | 2330 (67.91%) | 26 (36.11%) | |
| Current | 250 (18.93%) | 880 (17.75%) | 69 (23.39%) | | 16 (6.22%) | 192 (12.57%) | 34 (15.25%) | | 235 (21.76%) | 688 (20.05%) | 35 (48.61%) | |
| Used to | 158 (11.96%) | 660 (13.31%) | 52 (17.63%) | | 39 (16.18%) | 247 (16.18%) | 41 (18.39%) | | 119 (11.02%) | 413 (12.04%) | 11 (15.28%) | |
| **Alcohol status** | | | | 0.005 | | | | 0.002 | | | | <0.0001 |
| never drink | 622 (47.09%) | 2436 (49.13%) | 120 (40.68%) | | 122 (50.62%) | 808 (52.91%) | 110 (49.33%) | | 500 (46.30%) | 1628 (47.45%) | 10 (13.89%) | |
| current drinker | 392 (29.67%) | 1515 (30.56%) | 113 (38.31%) | | 29 (12.03%) | 283 (18.53%) | 55 (24.66%) | | 363 (33.61%) | 1232 (35.91%) | 58 (80.56%) | |
| former drinker | 307 (23.24%) | 1007 (20.31%) | 62 (21.02%) | | 90 (37.34%) | 436 (28.55%) | 58 (26.01%) | | 217 (20.09%) | 571 (16.64%) | 4 (5.56%) | |
| **Drug use** | | | | <0.0001 | | | | 0.035 | | | | 0.005 |
| No | 1201 (90.92%) | 4490 (90.56%) | 243 (82.37%) | | 212 (87.97%) | 1336 (87.49) | 179 (80.27%) | | 989 (91.57%) | 3154 (91.93%) | 64 (88.89%) | |
| Yes | 118 (8.93%) | 462 (9.32%) | 49 (16.61%) | | 28 (11.62%) | 187 (12.25%) | 42 (18.83%) | | 90 (8.33%) | 275 (8.02%) | 7 (9.72%) | |
| Don't know | 2 (0.15%) | 6 (0.12%) | 3 (1.02%) | | 1 (0.41%) | 4 (0.26%) | 2 (0.90%) | | 1 (0.09%) | 2 (0.06%) | 1 (1.39%) | |

## 3.4 Multivariable logistic regression analysis of substance use overall

The overall multivariable logistic regression model (which includes both countries) is presented in Table 4. This model found that individuals with a positive HIV status had 1.22 higher odds of substance use than those with a negative status (p=0.012, 95%CI 1.04-1.43). Those who were in younger age categories (<65) were less likely to take substances, 25-49 years having 0.73 odds (p=0.014, 95%CI 0.57-0.94) and 50-64 having 0.76 odds (p=0.020, 95%CI 0.61-0.96). The largest significant effect size was seen in the overall model between sex and substance use: males had 15.5 higher odds of substance use than females (p<0.0001, 95%CI 13.4-17.9). Those who were in the third socioeconomic quintile had a marginally protective odds ratio of 0.81 (p=0.088, 95%CI 0.64-1.03) versus those who were in the poorest first quintile. Marriage was a protective factor against substance use as all other marital status categories (except ' divorced with living partner') had increased odds of substance use when compared to marriage; the lowest being those whose 'partners have deceased' with an increased odds of 1.51 (p<0.0001, 95%CI 1.23-1.86) , and the highest being those who were 'separated but still living with their partners' having 2.68 increased odds of substance use (p<0.0001, 95%CI 2.03-3.53). Formal full-time employment was shown to have a protective factor with a 0.72 odds ratio of substance use compared to those who were unemployed (p=0.003, 95%CI 0.58-0.89). Informal employment and self-employment were shown to have an increased risk of substance use versus those who were unemployed, their odds ratios being 1.41 (p=0.0002, 95%CI 1.17-1.68) and 1.27 respectively (p=0.0089, 95%CI 1.06-1.52).

### *3.4.1 Multivariable logistic regression analysis of substance use in Kenya*

The multivariable logistic regression model for only Kenya is presented in Table 5. Kenyans with a HIV positive status had 1.49 higher odds of substance use when compared to those with a HIV negative status (p=0.013, 95%CI 1.09-2.03). Males showed a significant effect size, having 11.6 higher odds of substance use compared to females (p<0.0001, 95%CI 8.65-15.5). The third socioeconomic quintile had a marginally protective odds ratio of 0.7 (p=0.077, 95%CI 0.48-1.04) versus those who were in the poorest first quintile. Formal full-time employment was protective in Kenyans with a 0.41 odds ratio compared to

unemployment (p=0.0018, 95%CI 0.24-0.72). These four factors mirrored the trends seen in the overall logistic model. However, compared to marriage, only those who were 'separated with living partner' showed a 2.34 increased odds of substance use (p<0.0001. 95%CI 1.63-3.35). All other categories of marital status, age, highest level of education completed, and SES were not significant risk factors for substance use in the Kenyan model.

### *3.4.2 Multivariable logistic regression analysis of substance use in South Africa*

The multivariable logistic regression model for only South Africa is presented in Table 6. In the South African model only sex, age category, marital status and occupational status had significant associations with substance use. PLWHA had a 1.06 odds of substance use, showing that HIV status had about no effect on the likelihood of substance use, however p=0.54 (95%CI 0.88-1.28) indicating that this finding was not a significant association. South African males had a 17.7 higher odds of substance use compared to South African females (p<0.0001, 95%CI 14.9-21.1). Those who were younger in age (<65) were less likely to use substances, 25-49 years having 0.78 odds (p=0.087, 95%CI 0.59 – 1.04) and 50-64 having 0.75 odds ratio (p=0.019, 95%CI 0.59 – 0.95). All other types of marital status types had an increased odds of substance use when compared to marriage, the highest being 'separated with living partner' with 3.01 increased odds (p<0.0001, 95%CI 1.77-5.12) and the lowest being 'partner deceased' with an odds ratio of 1.58 (p=0.0012, 95%CI 1.20-2.10). Only the 'divorced with living partner' marital category showed no significant association with substance use. Full-time employment in the SA model was found to be not significant as a protective factor (aOR=0.98, p=0.91, 95%CI 0.75-1.28). Self-employment and informal employment were shown to carry greater risks of substance use, increasing odds more than two-fold (aOR=2.27, p<0.001, 95%CI 1.63-3.16; aOR= 1.50, p=0.0008, 95%CI 1.19-1.91 respectively), versus those who were unemployed. HIV status, highest level of education completed, and SES were not significantly associated with substance use in this model.

*Table 4: Multivariable logistic regression analysis of substance use in both countries (n=5872)*

| VARIABLES | Coefficient (β) | Odds Ratio | SE | z | p values | 95% CI |
|---|---|---|---|---|---|---|
| Substance use | | | | | | - |
| **HIV status,** Positive | 0.16 | 1.22** | (0.097) | 2.50 | 0.012 | 1.04 - 1.43 |
| **Age category,** 65 and older (ref) | | 1 | | | | |
| Age category, 25-49 | -0.31 | 0.73** | (0.093) | -2.46 | 0.014 | 0.57 - 0.94 |
| Age category, 50-64 | -0.27 | 0.76** | (0.089) | -2.32 | 0.020 | 0.61 - 0.96 |
| **Sex,** Male | 2.74 | 15.5*** | (1.15) | 37.0 | <0.0001 | 13.4 - 17.9 |
| **SES quintiles,** 1st (ref) | | 1 | | | | |
| SES quintiles, 2nd | -0.13 | 0.85 | (0.097) | -1.39 | 0.16 | 0.68 - 1.07 |
| SES quintiles, 3rd | -0.15 | 0.81* | (0.099) | -1.71 | 0.088 | 0.64 - 1.03 |
| SES quintiles, 4th | -0.15 | 0.84 | (0.095) | -1.58 | 0.11 | 0.67 - 1.04 |
| SES quintiles, 5th | -0.061 | 0.93 | (0.11) | -0.60 | 0.55 | 0.75 - 1.17 |
| **Highest level of education,** No formal education (ref) | | 1 | | | | |
| Highest level of education, Primary | -0.14 | 0.87 | (0.083) | -1.47 | 0.14 | 0.72 - 1.05 |
| Highest level of education, Secondary | -0.076 | 0.93 | (0.096) | -0.75 | 0.45 | 0.75 - 1.13 |
| Highest level of education, Tertiary | -0.068 | 0.85 | (0.16) | -0.87 | 0.38 | 0.58 - 1.23 |
| **Marital status**, Married (ref) | | 1 | | | | |
| Marital status, Living Together | 0.34 | 1.92*** | (0.26) | 4.79 | 1.7e-06 | 1.47 - 2.51 |
| Marital status, Never married or co-habited | 0.35 | 1.71*** | (0.18) | 4.94 | 7.7e-07 | 1.38 - 2.11 |
| Marital status, Divorced with living partner | 0.11 | 1.19 | (0.13) | 1.60 | 0.11 | 0.96 - 1.48 |
| Marital status, Separated with living partner | 0.45 | 2.68*** | (0.38) | 6.95 | <0.0001 | 2.03 - 3.53 |
| Marital status, Partner deceased | 0.26 | 1.51*** | (0.16) | 3.93 | 0.000087 | 1.23 - 1.86 |
| **Employment status**, Unemployed (ref) | | 1 | | | | |
| Employment status, Self-employed | 0.19 | 1.27*** | (0.12) | 2.62 | 0.0089 | 1.06 - 1.52 |
| Employment status, Formal full-time | -0.22 | 0.72*** | (0.080) | -2.99 | 0.0028 | 0.58 - 0.89 |
| Employment status, Part-time | 0.047 | 1.11 | (0.17) | 0.69 | 0.49 | 0.82 - 1.51 |
| Employment status, Informal | 0.26 | 1.41*** | (0.13) | 3.68 | 0.00023 | 1.17 - 1.68 |
| Constant | | 0.43*** | (0.061) | -5.95 | 2.7e-09 | 0.32 - 0.57 |

*** p<0.01, ** p<0.05, * p<0.1

*Table 5: Multivariable logistic regression analysis of substance use in Kenya (n=1765)*

| VARIABLES | Coefficient (β) | Odds Ratio | SE | z | p values | 95% CI |
|---|---|---|---|---|---|---|
| Substance use | | | | | | - |
| **HIV status,** Positive | 0.27 | 1.49** | (0.24) | 2.48 | 0.013 | 1.09 - 2.03 |
| **Age category,** 65 and older (ref) | | 1 | | | | |
| Age category, 25-49 | 0.49 | 1.65 | (1.80) | 0.46 | 0.64 | 0.20 - 13.9 |
| Age category, 50-64 | 0.56 | 1.77 | (1.92) | 0.52 | 0.60 | 0.21 - 14.9 |
| **Sex,** Male | 2.43 | 11.6*** | (1.71) | 16.5 | <0.0001 | 8.65 - 15.5 |
| **SES quintiles,** 1st (ref) | | 1 | | | | |
| SES quintiles, 2nd | -0.14 | 0.84 | (0.16) | -0.89 | 0.37 | 0.57 - 1.23 |
| SES quintiles, 3rd | -0.30 | 0.70* | (0.14) | -1.77 | 0.077 | 0.48 - 1.04 |
| SES quintiles, 4th | -0.27 | 0.72 | (0.15) | -1.62 | 0.11 | 0.48 - 1.07 |
| SES quintiles, 5th | -0.095 | 0.89 | (0.19) | -0.55 | 0.59 | 0.59 - 1.35 |
| **Highest level of education,** No formal education (ref) | | 1 | | | | |
| Highest level of education, Primary | 0.0027 | 1.00 | (0.22) | 0.012 | 0.99 | 0.65 - 1.54 |
| Highest level of education, Secondary | -0.15 | 0.85 | (0.20) | -0.70 | 0.48 | 0.54 - 1.34 |
| Highest level of education, Tertiary | -0.053 | 0.80 | (0.41) | -0.44 | 0.66 | 0.29 - 2.17 |
| **Marital status**, Married (ref) | | 1 | | | | |
| Marital status, Living Together | 0.13 | 1.58 | (0.66) | 1.09 | 0.28 | 0.70 - 3.56 |
| Marital status, Never married or co-habited | 0.083 | 1.23 | (0.36) | 0.73 | 0.47 | 0.70 - 2.18 |
| Marital status, Divorced with living partner | 0.091 | 1.36 | (0.49) | 0.84 | 0.40 | 0.67 - 2.76 |
| Marital status, Separated with living partner | 0.54 | 2.34*** | (0.43) | 4.62 | 3.9e-06 | 1.63 - 3.35 |
| Marital status, Partner deceased | | 1 | | | | |
| **Employment status**, Unemployed (ref) | 0.19 | 1.29 | (0.22) | 1.50 | 0.13 | 0.92 - 1.79 |
| Employment status, Self-employed | -0.23 | 0.79 | (0.19) | -0.96 | 0.33 | 0.50 - 1.27 |
| Employment status, Formal full-time | -0.61 | 0.41*** | (0.12) | -3.13 | 0.0018 | 0.24 - 0.72 |
| Employment status, Part-time | -0.13 | 0.65 | (0.28) | -1.01 | 0.31 | 0.28 - 1.51 |
| Employment status, Informal | -0.00026 | 1.00 | (0.25) | -0.0011 | 1.00 | 0.61 - 1.63 |
| Constant | | 0.29 | (0.33) | -1.10 | 0.27 | 0.032 - 2.62 |

*** p<0.01, ** p<0.05, * p<0.1

*Table 6: Multivariable logistic regression analysis of substance use in South Africa (n=4107)*

| VARIABLES | Coefficient (β) | Odds Ratio | SE | z | p values | 95% CI |
|---|---|---|---|---|---|---|
| Substance use | | | | | | - |
| **HIV status,** Positive | 0.051 | 1.06 | (0.10) | 0.62 | 0.54 | 0.88 - 1.28 |
| **Age category,** 65 and older (ref) | | 1 | | | | |
| Age category, 25-49 | -0.23 | 0.78* | (0.11) | -1.71 | 0.087 | 0.59 - 1.04 |
| Age category, 50-64 | -0.29 | 0.75** | (0.092) | -2.35 | 0.019 | 0.59 - 0.95 |
| **Sex,** Male | 2.88 | 17.7*** | (1.58) | 32.1 | <0.0001 | 14.9 - 21.1 |
| **SES quintiles,** 1st (ref) | | 1 | | | | |
| SES quintiles, 2nd | -0.12 | 0.87 | (0.12) | -1.01 | 0.31 | 0.66 - 1.14 |
| SES quintiles, 3rd | -0.022 | 0.97 | (0.15) | -0.20 | 0.84 | 0.71 - 1.32 |
| SES quintiles, 4th | -0.10 | 0.89 | (0.12) | -0.85 | 0.40 | 0.67 - 1.17 |
| SES quintiles, 5th | -0.057 | 0.94 | (0.13) | -0.44 | 0.66 | 0.71 - 1.24 |
| **Highest level of education,** No formal education (ref) | | 1 | | | | |
| Highest level of education, Primary | -0.16 | 0.84 | (0.093) | -1.55 | 0.12 | 0.68 - 1.05 |
| Highest level of education, Secondary | -0.056 | 0.94 | (0.11) | -0.47 | 0.64 | 0.75 - 1.20 |
| Highest level of education, Tertiary | -0.18 | 0.67* | (0.15) | -1.81 | 0.070 | 0.44 - 1.03 |
| **Marital status**, Married (ref) | | 1 | | | | |
| Marital status, Living Together | 0.37 | 1.84*** | (0.28) | 4.06 | 0.000050 | 1.37 - 2.48 |
| Marital status, Never married or co-habited | 0.34 | 1.59*** | (0.20) | 3.76 | 0.00017 | 1.25 - 2.02 |
| Marital status, Divorced with living partner | 0.11 | 1.17 | (0.14) | 1.30 | 0.19 | 0.92 - 1.48 |
| Marital status, Separated with living partner | 0.37 | 3.01*** | (0.82) | 4.06 | 0.000050 | 1.77 - 5.12 |
| Marital status, Partner deceased | 0.26 | 1.59*** | (0.23) | 3.24 | 0.0012 | 1.20 - 2.10 |
| **Employment status**, Unemployed (ref) | | 1 | | | | |
| Employment status, Self-employed | 0.47 | 2.27*** | (0.38) | 4.82 | 1.4e-06 | 1.63 - 3.16 |
| Employment status, Formal full-time | -0.010 | 0.98 | (0.13) | -0.12 | 0.91 | 0.75 - 1.28 |
| Employment status, Part-time | 0.095 | 1.22 | (0.21) | 1.15 | 0.25 | 0.87 - 1.70 |
| Employment status, Informal | 0.27 | 1.50*** | (0.18) | 3.37 | 0.00076 | 1.19 - 1.91 |
| Constant | | 0.40*** | (0.064) | -5.68 | 1.3e-08 | 0.30 - 0.55 |

*** p<0.01, ** p<0.05, * p<0.1

### *3.4.3 Sensitivity Analysis*

When employment status was excluded from the models, the overall model experienced 3 changes in significant factors. Completion of tertiary education became a significant protective factor showing a 0.70 odds of substance use (aOR=0.70, p=0.046, 95%CI: 0.49-0.99), when compared to those with no formal education completed. 'Divorced with living partner' became a strongly significant factor in this model with a 1.33 higher odds of substance use compared to those who were married (aOR=1.33, p=0.006, 95%CI: 1.08-1.62). Lastly age was no longer significant in the overall model.

The Kenyan specific model changed with regards to the third and fourth SES quintiles. These two quintiles showed a protective factor against substance use with a 0.66 aOR (p=0.035, 95%CI: 0.45-0.97) and 0.63 aOR (p=0.024, 95%CI: 0.43-0.94) respectively when compared to those in the first SES quintile.

The South African specific model changed with regards to completion of primary and tertiary education showing a protective 0.81 aOR (p=0.034, 95%CI: 0.666-0.98) and 0.65 aOR (p=0.033, 95%CI: 0.44-0.97) respectively, when compared to those who had completed no formal education.

Despite these changes, employment status was chosen to be included in the final models as the literature supports it as an important associated factor (Hatcher et al., 2022; Jaguga et al., 2022).

# CHAPTER 4

This final chapter discusses (4.1) and compares the results of the analysis with current literature on tobacco, alcohol, and injectable drug use in HIV positive populations living in South Africa and Kenya. Key points highlighted around prevalence and risk factors leads to final conclusions (4.2) regarding further studies. The chapter closes with a discussion on the limitations of the study (4.3).

# 4. DISCUSSION AND CONCLUSIONS

## 4.1 Discussion

The prevalence of substance use (alcohol use, tobacco smoking and drug use) in the overall sample was 54.30%. This prevalence was similar in Kenya (51.33%) and South Africa (SA) (55.60%).

In a national survey on drugs and substance use in Kenya (NACADA), the prevalence of using at least one substance was 17.5% amongst 15–65-year-olds, which – although lower than the prevalence rate found in this analysis – is not comparable to our study findings due to different age ranges (NACADA, 2023). The NACADA survey does not report any comparable estimates for the 40–60-year-old age group, as the oldest age group reported is "36+". For the 36 and older age group the NACADA survey only reports individual prevalence estimates for each substance type and does not provide an overall estimate.

In South Africa there is no comparable combined national prevalence estimate, however there are individual studies or reports that have estimated the national prevalences for individual substance types: harmful alcohol use 10.3%, tobacco use 20.3% and illicit drug use 8.6-10.0%(Mutai et al., 2024; Pengpid et al., 2021; World Health Organization, 2021)(Mutai et al., 2024; Pengpid et al., 2021; World Health Organization, 2021). All of these national estimates are lower than the prevalence rate found in this analysis, but we must use caution as the studies report for the 15 and older age range. Only Pengpid *et al* (2021) reported a sub-stratified prevalence estimate for harmful alcohol use and drug use for these older age groups:

35-44 olds (10.4% harmful alcohol use and 7.9% drug use), 45-54 (9.0% and 6.4% respectively) and 55+ (5.1% and 4.4% respectively).

The prevalence of HIV in the overall sample was 20.94%. In Kenya HIV prevalence was found to be 13.66%, and in South Africa 23.35%. These HIV prevalences are higher than the national prevalence estimates reported by the SABSSM V in 2019 (14.0%) and KENPHIA in 2022 (4.9%) (Kenyan Ministry of Health, 2022; Simbayi et al., 2019).

The above findings on HIV and substance use could be attributed to the geographic location of where participants were recruited from for the primary AWI-Gen study: if these regions (Nairobi in Kenya and Dikgale, Agincourt and Soweto in South Africa) had a higher-than-average HIV prevalence and substance use prevalence this could account for higher prevalence rates than the national estimates in the literature. In addition, non-random sampling methods used in the primary AWI-Gen study could have introduced bias as the authors report that in some sites, such as Agincourt, previous research participants were invited to participate in the primary study (Ali et al., 2018)(Ali et al., 2018). Those research participants may have introduced a selection bias. In contrast, the SABSSM V used a multistage stratified random cluster sampling design and the KENPHIA used a two-stage, stratified cluster sample design. Both of which would have introduced far less bias than the research participant selection bias. The AWI-Gen study also had a much smaller sample size than the SABSSM V and the KENPHIA, n=10 703 versus n=36 609 and n=30 384 respectively. The differences in sample sizes and sample methodologies could also account for the differences in HIV and substance use prevalence estimates.

HIV status and substance use was found to be positively associated with each other, corroborating what was already found across the literature (Fisher et al., 2007; Hammer et al., 2018; Hatcher et al., 2022; Jaguga et al., 2022; Kuteesa et al., 2019; Pithey & Parry, 2009; UNAIDS, 2020, 2022c, 2022d). Specifically in this study it was found that PLWHA had a 1.22 greater odds of substance use than those who were HIV negative in the overall sample (p=0.012, 95%CI 1.04-1.43). In Kenya, PLWHA had a 1.49 higher odds of substance use than those who were HIV negative (p=0.013, 95%CI 1.09-2.03). In South Africa, there was no significant association found between HIV status and substance use (aOR=1.06, p=0.54, 95%CI 0.88-1.28). In South Africa there may have been underreporting of both substance use and HIV status as both relied on self-report and were thus influenced by social desirability bias (e.g. stigma and fear of discrimination) and recall bias. Mooney, *et al* (2018) investigated

inconsistencies in HIV self-reporting and found that participants misunderstood their treatment drugs or the types of tests they have received at a clinic, and this led to unintentional under reporting of HIV status. Mooney *et al,* (2018) found that insufficient medical explanations from the healthcare worker can leave patients misinformed about their status. If participants were not asked about their HIV status in their home language, language barriers have also been cited as a possible cause for misreporting and errors in recording (Metz et al., 2024).

The factors that were found to be associated with substance use in the overall logistic model was HIV status, sex, age, marital status, and employment status. Being employed full-time (aOR=0.72, p=0.0028, 95%CI 0.58-0.89), being married (versus the four other marital statuses) and being younger than 65 were shown to be protective factors against substance use. Boredom, lack of structure and lack of daily routine, has been highlighted to be an important contributing factor to substance use initiation and relapse (Magidson et al., 2020), thus it aligns that full-time employment – which fills one's time with structure, routine and often purpose – would be a possible protective factor against substance use. The exception to this would be high risk occupational groups such as commercial sex workers who, when formally employed, use drugs such as cocaine and benzodiazepines to relieve stress and function at work (Phyllys et al., 2022). Commercial sex workers who are informally employed or unemployed use less drugs than those who are formally employed; with 40% reporting it is due to drug availability or lack of money (Phyllys et al., 2022).

Older individuals have had more time and more opportunities to use substances, than an individual who is younger in years; thus, younger age being a protective factor might only be alluding to this temporal affect. Phyllys *et al* (2022) found that alcohol usage increased significantly with age, but tobacco usage decreased with age. Married adults have been found in the literature to use less alcohol, tobacco and cannabis as compared to divorced and separated adults, as it is hypothesized that the social support of marriage assists in the reduction of substance use (Kahle et al., 2020; Menasco & Blair, 2016; Salvatore et al., 2020).

The largest significant risk factor for substance use across all three models was being male, with an increased odds of 15.5 in the overall model (p<0.0001, 95%CI 13.4 - 17.9), 11.6 in Kenya (p<0.0001, 95%CI 8.65 - 15.5) and 17.7 in South Africa (p<0.0001, 95%CI 14.9-21.1). It is well documented in the literature that men are more likely to use substances than

women – whether that be alcohol binge drinking, tobacco smoking, or illicit drug use – and that they have a higher prevalence of AUD than women (Hammer et al., 2018; Murphy, Liu and Parascandola, 2019; Scheibe et al., 2020; Stanton et al., 2021; Hatcher et al., 2022).

In the Kenyan logistic model HIV status, sex, marital status, and employment status were found to be associated with substance use. Full-time employment was a significant protective factor against substance use in the Kenyan model – reducing the likelihood of substance use by 59% (aOR=0.41, p=0.0018, 95%CI 0.24-0.72). This is perhaps because full-time employment does not allow for much time for boredom (Magidson et al., 2020) and financial stressors are lessened due to employment (Paschen-Wolff et al., 2019). Full-time employment also gives individuals access to additional work resources to cope with stress, such as an employee wellness program and a social support network. For those individuals who were separated from their partners (aOR=2.34, p<0.0001, 95%CI 1.63-3.35), they were twice as likely to use substances compared to those who were married – this finding is consistent with the literature that supports marriage as a protective factor (Kahle et al., 2020; Menasco & Blair, 2016; Salvatore et al., 2020). This is perhaps due to the emotional distress of being separated from their partner and having that reduced lack of social support drives increased dependency on substances as a coping strategy (Kahle et al., 2020; Menasco & Blair, 2016; Salvatore et al., 2020; Samokhvalova et al., 2022) .

In the South African logistic model age, sex, marital status, and employment status were the four factors found to be associated with substance use. Age and marriage were protective factors. However, differing from the Kenyan model and overall model, full-time employment in SA was found to be not significant as a protective factor (aOR=0.98, p=0.91, 95%CI 0.75-1.28). Self-employment and informal employment were shown to carry greater risks of substance use, increasing odds by almost two-fold (aOR=2.27, p<0.001, 95%CI 1.63-3.16; aOR= 1.50, p=0.0008, 95%CI 1.19-1.91 respectively), versus those who were unemployed. This is perhaps due to the highly stressful nature of self-employment and informal employment. Cohabiting, never married or lived together, being separated from a living partner and having a deceased partner all held significant greater risk of using substances than being married – increasing the odds of substance usage between 1.59 - 3.01.

## 4.2 Conclusions

The study's findings, considered within the broader context of the existing literature, underscore the need for targeted, comprehensive substance use treatment interventions integrated into ART care and specific to the country's population. Specifically, interventions and programmes should be targeted towards males as they are the group most at risk of substance misuse behaviours. Specifically, substance misuse health promotion initiatives, preventative education, mental health and community talks should be tailored toward men to address their disproportionately high risk. Training and sensitisation should highlight for staff and communities that substance misuse is often a mental health coping mechanism and a factor in risky sexual behaviour. The implementation of the substance misuse interventions should be tailored to the unique factors that are associated with each type of substance misuse in each country. Substance misuse treatment should become a necessary part of integrated HIV care as the prevalence of substance misuse in PLWHA in this study and across the literature is high. Substance misuse treatment in HIV care settings can assist to reduce HIV risk in HIV negative patients (who are for example attending for PrEP or family planning services), and to reduce ART non-adherence and ART defaulting, in turn working to reduce ART regimen resistances, and decrease morbidity and mortality in PLWHA. Substance misuse for PLWHA treatment policies should consider the social and gendered norms (as substance use prevalence and correlates differ by gender), as well as the structural and contextual factors of the country (e.g. policies and taxes) to ensure solutions that are engaging, meaningful and feasible (Magidson et al., 2020).

Future research should focus on evaluating the effectiveness of integrated care models that simultaneously address substance misuse and HIV, with a particular emphasis on gender-sensitive approaches and socio-economic empowerment as key components of effective interventions. More research on non-injectable drug types in SSA and systematic reviews of substance use in South Africa, smoking and HIV in SSA, IDU and HIV in SSA, is needed as well to fill gaps in the literature.

## 4.3 Limitations

Some of the limitations of a cross-sectional dataset includes the inability to infer causality of the HIV outcome or substance use outcome due to there being no temporality in the data. One is unable to tell if exposure or outcome came first in the causality chain. Also, in our cross-sectional data one cannot determine incidence of HIV and substance use, only prevalence estimates of these two factors. Limitations of secondary data analysis include having no control over the type of data collected, the quality of the data, missing data, collection methods/tools used (how it was collected), sample size, or sample population.

The primary study relied on HIV self-reporting for HIV status, which has several drawbacks. Self-reporting can lead to under reporting of HIV prevalence due to social desirability bias (stigma and fear of discrimination) or recall bias. Common mistakes such as recording errors or incorrect statements can occur when the HIV status consult does not occur in the patient's home language or there are other language challenges such as the reporting forms being in a different language (Metz et al., 2024). Mooney, et al (2018) investigated inconsistencies in HIV self-reporting and found that participants misunderstood their treatment drugs or the types of tests they have received at a clinic, and this led to unintentional under reporting of HIV status. Self-reported status relies on patient knowledge from clear patient-clinician communication, however if this communication is vague and lacks clear medical explanations, this can be another reason for unreliable self-reported HIV status (Mooney et al., 2018).

The sampling methodology for the Soweto and Agincourt sites were not completely randomized, as the authors of the primary study invited and recruited research participants from other pre-existing studies at those study sites. This may have introduced a type of selection bias called volunteer bias or self-selection bias, whereby the participants disproportionately select themselves into a group creating a sample that possesses traits that differ from non-volunteers (Elston, 2021; Jordan et al., 2013). In clinical studies, these traits are often associated with socioeconomic status, greater willingness to comply with the study intervention, and better outcomes (Elston, 2021). Volunteers tend to not be entirely representative of the population that they were sampled from.

A limitation with the way drug usage data was collected in the primary study is that current and past usage was not disaggregated. Thus, to compare drug usage with alcohol and tobacco

usage, current and past usage had to be combined into a binary outcome variable which resulted in a loss of detail in the data. In addition, the population studied in this secondary data analysis were between the ages of 40 and 60 years, which is not a representative sample of South Africa and Kenya. These two countries are still developing, and their populations are skewed towards the younger demographic.

The data set was incomplete for many key variables, with n=1345 participants having no data recorded for any type of substance use, n=744 participants missing information on their HIV status and n=401 participants missing information on their employment status. Missing data can reduce the statistical power of the study as it results in a smaller sample size. This could increase the risk of a type 2 error (failing to reject the null hypothesis). A possible reason for not finding a significant association between substance use and HIV status in the SA logistic model may have been influenced by n=524 HIV status data missing from the Soweto cohort. Missing data introduces bias into the study, especially if the nature of the missing data is not random. It is difficult to assess the true nature of missing data in a secondary data analysis as we were not present during primary data collection. Missing data may also reduce the representativeness of the sample and thus reduce the generalizability of the study findings.

The only site from Kenya that contributed data was an urban community research site in Nairobi. From South Africa there were two rural community research sites (Agincourt and Dikgale) and one urban community research site (Soweto). This further reduces the generalizability of the Kenyan findings to only urban communities, as there was no representative sample from a Kenyan rural community site. Whilst South Africa had more of a balance with both urban and rural communities sampled, the urban community of Soweto had n=524 HIV status data missing, which biases the findings of the South African model more towards the rural communities. In addition, the lack of a Kenyan rural community sample prevented a comparison between SA and Kenya HIV status and substance use in urban and rural areas. There were three sites from South Africa and only one site from Kenya, resulting in a greater number of South Africans being recruited for the study and a smaller number of Kenyans. The discrepancy in sample sizes between South Africa and Kenya biases the findings of the data to be more robust for the South African sample, as a larger sample size increases the power of the statistical tests.

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# Appendix A: HREC Ethics Certificate

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

**Office of the Deputy Vice-Chancellor (Research and Innovation)**

| | |
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| **TO:** | Ms S Jack<br>School of Public Health<br>Division of Epidemiology and Biostatistics<br>Medical School<br>University<br><br>E-mail: samantha.jack@gmail.com |
| **CC:** | Supervisor: Drs S Mall, I Maphosa and K Wilson<br><Samaya.Mall@wits.ac.za><br>and <HREC-Medical Research Office@wits.ac.za> |
| **FROM:** | Mr Iain Burns<br>Human Research Ethics Committee (Medical)<br>Tel: 011 717 1252<br><br>E-mail: Iain.Burns@wits.ac.za |
| **DATE:** | 2021/12/23 |
| **REF:** | R14/49 |
| **PROTOCOL NO:** | **M210873** (This is your ethics application reference number. Please quote it in all enquiries, oral or written, relating to this study.) |
| **PROJECT TITLE:** | *The association between substance use and HIV in two sub-Saharan African countries, 2014 - 2016* |

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 Government funding of the University.

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# Appendix B: Plagiarism Declaration Report

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