UNIVERSITY OF NAIROBI

COLLEGE OF HEALTH SCIENCES

DEPARTMENT OF CLINICAL MEDICINE AND THERAPEUTICS

QUALITY OF SLEEP AND RISK OF OBSTRUCTIVE SLEEP APNEA IN ADULTS WITH HIV INFECTION AT KENYATTA NATIONAL HOSPITAL

DR. MUTAI EBBY CHELANGAT

H58/6771/2017

A DISSERTATION SUBMITTED IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE DEGREE OF MASTER OF MEDICINE IN INTERNAL MEDICINE

2022

DECLARATION

This research dissertation is my original work and has not been presented for a degree in any other university.

Signature..... Date....23/05/2022.....

Dr. Ebby Chelangat Mutai

APPROVAL BY SUPERVISORS

Dr. Jared. O. Mecha, MBChB, M. Med, MSc-RM (Lond.), MPH (Berkeley)

Consultant Physician / Pulmonologist, Respiratory & Infectious Disease Specialist,

Lecturer, Department of Clinical Medicine and Therapeutics,

University of Nairobi

Signature..... Date..23/05/22.

Prof. Erastus. O. Amayo

MBChB, M. Med, FAAN, FRCPE, Certificate in Tropical Medicine, Certificate in Health and Behavior Research (Harvard)

Consultant Physician / Neurologist

Professor, Department of Clinical Medicine and Therapeutics,

University of Nairobi.

Signature..... Date.....29/5/2022

DEDICATION

I dedicate this work to my dear parents Charles Mutai and Martha Mutai, who have loved and supported me unconditionally, and taught me to work hard for the things I aspire to achieve. This work is also dedicated to my brothers Kevin Yegon and Brian Yegon, who have always had my back. My love and gratitude for you all has no bounds.

ACKNOWLEDGEMENT

I would like to thank my supervisors who were very supportive and offered me guidance throughout the research process.

Many thanks to my family for their constant encouragement and prayers, always believing in me, and pushing me on in my endeavors.

I would also like to thank all my friends and colleagues who have been a great support system, encouraging and walking with me along the way.

Last but not least, I would like to thank God Almighty, my creator and source of strength, in whom I live and move and have my being.

TABLE OF CONTENTS

DECLARATION ii
APPROVAL BY SUPERVISORS iii
DEDICATION iv
ACKNOWLEDGEMENT v
TABLE OF CONTENTS vi
ABBREVIATIONS x
DEFINITION OF KEY TERMS xi
LIST OF TABLES xii
LIST OF FIGURES xiii
ABSTRACT xiv
1 CHAPTER ONE: INTRODUCTION 1
1.1 Background 1
2 CHAPTER TWO: LITERATURE REVIEW 3
2.1 Introduction 3
2.2 The structure of sleep 3
2.3 Epidemiology of poor sleep quality and sleep disorders in HIV 4
2.3.1 The burden of poor quality of sleep 6
2.3.2 Insomnia 6
2.3.3 Breathing-related sleep disorders 8
2.4 Mechanisms of poor sleep quality and sleep disturbances in HIV infection 12
2.4.1 HIV-specific factors 12
2.4.2 Psychological factors 16
2.4.3 Sociodemographic factors 16
2.5 Implications of poor quality of sleep and sleep disorders on persons with HIV 17
2.5.1 Increased risk of metabolic and cardiovascular diseases 17
2.5.2 Development of psychiatric disorders 19
2.5.3 Cognitive Impairment 19
2.5.4 Poor adherence 19
2.5.5 Impact on quality of life 20
2.6 Conceptual framework 22
2.7 Assessing sleep quality and screening for sleep disorders 23
2.7.1 Clinical Interviews 24

2.7.2 Sleep Diary 24
2.7.3 Actigraphy 24
2.7.4 Polysomnography (PSG) 25
2.7.5 Multiple Sleep Latency Test and Maintenance of Wakefulness Test 25
2.7.6 Sleep Questionnaires 26
2.8 Study justification 27
2.9 Research question 28
2.10 Broad objective 28
2.10.1 Specific objectives: 28
2.10.2 Secondary objectives: 28
3 CHAPTER THREE: METHODOLOGY 29
3.1 Study design 29
3.2 Study population 29
3.3 Study site 29
3.4 Case definition 29
3.5 Participant selection 30
3.5.1 Inclusion criteria: 30
3.5.2 Exclusion criteria: 30
3.6 Sample size 31
3.7 Sampling procedure 31
3.8 Recruitment and consenting procedure 31
3.9 Data collection tools and procedures 32
3.9.1 Data collection tools 32
3.9.2 Data collection procedures 32
3.10 Definition of terms 34
3.11 Quality assurance 34
3.12 Data management and analysis 34
3.13 Ethical Considerations 35
4 CHAPTER FOUR: RESULTS 37
4.1 Introduction 37
4.2 Descriptive analysis of the findings 38
4.2.1 Age distribution of the respondents 38
4.2.2 Demographic characteristics of HIV positive patients attending clinic at Kenyatta National Hospital 38

4.2.3 Clinical characteristics of HIV positive patients attending clinic at Kenyatta National Hospital 40
4.2.4 Treatment regimen among respondents 41
4.2.5 Presence of comorbidities among respondents 42
4.2.6 Assessment of anxiety and depression among HIV positive patients attending clinic at Kenyatta National Hospital 42
4.2.7 The prevalence of poor sleep quality in patients with HIV using the Pittsburgh Sleep Quality Index 43
4.2.8 Quality of sleep: component scores of the PSQI in patients with HIV 43
4.2.9 The burden of high risk for obstructive sleep apnea in patients with HIV using the STOP-BANG questionnaire 45
4.3 Bivariate analysis of the findings 45
4.3.1 The association between depression, anxiety, and quality of sleep in patients with HIV attending the HIV clinic at KNH. 45
4.3.2 Association between patient demographic characteristics and poor sleep quality . 46
4.3.3 Association between disease characteristics and poor sleep quality 47
4.3.4 Association between patient demographic characteristics and OSA 48
4.3.5 Association between disease characteristics and OSA 49
4.4 Multivariable analysis of the findings 51
4.4.1 Independent factors associated with poor sleep quality 51
4.4.2 Independent factors associated with obstructive sleep apnea 52
5 CHAPTER FIVE: DISCUSSION, CONCLUSION AND RECOMMENDATIONS 54
5.1 DISCUSSION 54
5.1.1 Quality of sleep of adults with HIV infection 54
5.1.2 Risk of obstructive sleep apnea in adults with HIV infection 55
5.1.3 Association between quality of sleep and depression in adults with HIV infection 56
5.1.4 Association between quality of sleep and anxiety in adults with HIV infection 57
5.1.5 Factors associated with poor sleep quality and high risk for obstructive sleep apnea 58
5.2 CONCLUSION 65
5.3 STUDY STRENGTHS 65
5.4 STUDY LIMITATIONS 65
5.5 RECOMMENDATIONS 65
REFERENCES 67
APPENDICES 79
Appendix 1: Screening proforma 79

Appendix 2: Participant information and consent form 80
Appendix 3: Ridhaa ya Kiswahili 84
Appendix 4: Study Proforma 87
Appendix 5: Proforma ya Utafiti 96
Appendix 6: Time frame 102
Appendix 7: Budget estimation and justification 103
Appendix 6: Similarity Report 105

ABBREVIATIONS

AIDS:	Acquired immunodeficiency syndrome
HAART:	Highly active antiretroviral therapy
ARV:	Antiretroviral
ART:	Antiretroviral therapy
BMI:	Body mass index
CCC:	Comprehensive care clinic
CVD:	Cardiovascular disease
HIV:	Human immunodeficiency virus
PLHIV:	People living with HIV
INSTI:	Integrase strand transfer inhibitor
NNRTI:	Non-nucleoside reverse transcriptase inhibitor
NRTI:	Nucleoside reverse transcriptase inhibitor
PI:	Protease inhibitor
PLHIV:	People living with HIV
PSQI:	Pittsburgh sleep quality index
UON:	University of Nairobi
VL:	Viral load
SPSS:	Statistical package for social sciences
OSA:	Obstructive sleep apnea
PSQI:	Pittsburgh Sleep Quality Index
SBQ:	STOP BANG questionnaire
PHQ-9:	Patient health questionnaire-9
GAD-7:	Generalized anxiety disorder 7-item scale
USA:	United States of America

DEFINITION OF KEY TERMS

Quality of sleep: this is defined as one's perception of satisfaction with their sleep experience, and this encompasses aspects of sleep initiation, sleep maintenance, sleep quantity, and refreshment upon awakening.

Sleep disorder: a clinical condition characterized by disruption of the normal patterns of sleep.

Obstructive sleep apnea: a sleep disorder characterized by recurrent cessation or reduction in airflow in the presence of breathing effort due to collapse of the upper airway.

LIST OF TABLES

Table 1: List of PSQI Studies 6
Table 2:Types of sleep questionnaires 26
Table 3:Demographic characteristics of HIV positive patients attending clinic at Kenyatta National Hospital 39
Table 4: Clinical characteristics of HIV positive patients attending clinic at Kenyatta National Hospital 40
Table 5:Treatment regimen among respondents 41
Table 6: Presence of comorbidities among respondents 42
Table 7 (a): Assessment of anxiety among the participants 43
Table 7 (b): Assessment of depression among the participants 43
Table 8: The prevalence of poor sleep quality in patients with HIV. 43
Table 9: Quality of sleep: component scores of the PSQI in patients with HIV 44
Table 10:The burden of high-risk obstructive sleep apnea in patients with HIV. 45
Table 11:The association between depression, anxiety, and quality of sleep in patients with HIV 45
Table 12:Association between patient demographic characteristics and poor sleep quality 46
Table 13:The relationship between disease characteristics and poor sleep quality 47
Table 14:Association between patient demographic characteristics and OSA 49
Table 15:Association between disease characteristics and OSA 50
Table 16:Independent factors associated with poor sleep quality 52
Table 17: Schedule of planned activities 102
Table 18:Budget estimation 103

LIST OF FIGURES

Figure 1:Implications of sleep disturbances 21
Figure 2: Conceptual Framework 22
Figure 3:Taxonomy of sleep detection methods 23
Figure 4: Study Flow chart 37
Figure 5:Age distribution 38

ABSTRACT

Background: Sleep disorders and poor sleep quality are more prevalent among HIV patients, with rates ranging from 30 percent to 100 percent, compared to 13 percent to 30 percent universally. In Kenya, there is a scarcity of data on sleep disorders, both in the general population and among people living with HIV (PLHIV). The main purpose of this study was to determine the quality of sleep and risk of obstructive sleep apnea in adult HIV infected patients attending the Kenyatta National Hospital's HIV Clinic.

Methodology: This was a cross-sectional study conducted in a hospital setting. The study site was the KNH HIV Clinic. HIV-positive adults aged 18 and above made up the study population. Participants who met the eligibility criteria and provided written informed consent were recruited into the study. The Pittsburgh Sleep Quality Index (PSQI), the STOP-BANG Questionnaire (SBQ), the Generalized Anxiety Disorder Questionnaire (GAD-7), and the Patient Health Questionnaire-9 (PHQ-9) were used to measure sleep quality, risk of obstructive sleep apnea (OSA), anxiety, and depression, respectively. Data was entered and managed in epidata version 3.1 and then exported to SPSS version 26.0 statistical software for analysis. Quality of sleep and risk for OSA were calculated and presented as percentages with 95% confidence interval. Chi-square or Fischer's exact test were conducted to determine bivariable associations. Logistic regression was used in multivariate analysis. All statistical tests were performed at a significance level of 5%.

Results: 312 participants were recruited into the study. 59.6% of the respondents had poor sleep quality while 58.7% of the respondents had high risk of obstructive sleep apnea. 43.3% of patients had anxiety while 31.4% had depression. On multivariate analysis, having a comorbidity, anxiety, or depression, was independently associated with poor sleep quality. Male gender, increase in age, body mass index and neck circumference were independently associated with high risk of OSA.

Conclusion: Poor quality of sleep is quite common among people living with HIV. Risk for obstructive sleep apnea is also high in this patient cohort. Early recognition and treatment of sleep disturbances could aid in overall improvement of health and quality of life.

1 CHAPTER ONE: INTRODUCTION

1.1 Background

It is estimated that globally, approximately thirty eight million persons are living with Human immune-deficiency virus (1). By the end of 2019, there were approximately 75.7 million infections since the pandemic began with associated 32.7 million AIDS related deaths (1). In Kenya, there are about 1.6 million persons living with HIV (2).

There has been significant decline in HIV-related morbidity and mortality since the advent of highly active antiretroviral therapy. Since the peak in 2004, AIDS-related deaths have decreased by 60% (1), turning HIV disease into a manageable chronic illness in patients who achieve sustained virologic suppression. Despite this, persons living with HIV remain at risk of mortality at a rate three to six times higher than the general population (3). Additionally, with improved survival, PLHIV are now at increased risk of age-related non-communicable disorders (4).

Sleep is affected by and affects both non-communicable and infectious diseases. The association between HIV disease and sleep is bi-directional, in that HIV disease can bring about sleep disturbances, and sleep disturbances can also affect the course of HIV disease. HIV infection is significantly associated with low quality of sleep. Sleep disturbances occur more commonly in the HIV population, with the prevalence of 30% to 100% (5), compared to 13% to 30% in the general population (6). Studies have shown that sleep disturbances occur early and can persist throughout HIV infection, whether the infection is left untreated, is advanced, or is chronic and controlled (7). Impairment of sleep quality is linked to cognitive dysfunction and psychiatric disorders. A link also exists between poor sleep quality in HIV patients and non-adherence to treatment and low quality of life as a whole. Though sleep disorders are common in HIV infection, they are mostly underdiagnosed and untreated.

Numerous studies have demonstrated the influence of sleep on health (8). Sleep disorders such as obstructive sleep apnea increase cardiovascular risk. In addition to cardiometabolic diseases, sleep disturbances could also contribute to the onset and exacerbation of psychiatric illnesses, neurocognitive impairment, and non-adherence to treatment. Furthermore, poor sleep leads to lower productivity, straining both social and economic resources and adversely affecting health-related quality of life overall.

Data on sleep disorders in Kenya in both the general population and among people living with HIV is scarce. This information gap limits the development of specific interventions to tackle the unique challenges faced in managing HIV illness as a chronic disease. Identifying sleep disturbances in PLHIV will aid in the treatment and prevention of these disturbances and improve HIV treatment outcomes and overall quality of life. It is against this background that this study set out to determine the burden of poor quality of sleep and risk for obstructive sleep apnea among PLHIV followed up at the HIV Clinic at Kenyatta National Hospital.

2 CHAPTER TWO: LITERATURE REVIEW

2.1 Introduction

The number of people living with HIV/AIDS was estimated at 38 million by 2019 globally, with majority being from Africa (54% from Eastern Africa and 13% from West and Central Africa). However, deaths associated with AIDS have reduced by 60% over the years since they peaked in 2004. This has been immensely attributable to the scale up of antiretroviral therapy (ART) (1). The effective use of ART has seen HIV evolve into a manageable chronic condition. With this evolution, new issues are emerging about HIV-associated morbidity and mortality.

Sleep disturbances are common and debilitating yet are frequently underdiagnosed, particularly among persons living with HIV. Sleep disorders in HIV-infected people have been associated with an increase in cardiovascular risk, non-adherence, psychiatric illnesses, cognitive impairment, and various other deleterious outcomes. It may be argued that the greater incidence of sleep disturbances among PLHIV is solely secondary comorbid psychiatric disorders such as depression and anxiety. However, studies have suggested the role of other etiologies such as neuronal injury, comorbid medical conditions, the effect of ART, and psychosocial stressors (9).

2.2 The structure of sleep

Normal sleep is broadly categorized into two stages: rapid eye movement (REM) sleep and non-rapid eye movement sleep (NREM).

Rapid eye movement (REM) sleep and the nonrapid eye movement sleep (NREM) are two major categories of normal which are subsequently classified into three other categories which include N1, N2, and N3. REM and NREM sleep cycles alternate during the night, with one cycle lasting 90 to 120 minutes. Each night, there are approximately 4 to 5 cycles. NREM sleep predominantly takes up the first two-thirds of the night, while the last third largely comprises of REM sleep.

After the onset of sleep, progression is first through the NREM stages N1-N3 sleep sequentially for 45-60 minutes. **N1** sleep is a 'transitional' state (from being awake to falling asleep). It takes up 2% to 5% of the total sleep duration and is defined by low amplitude, fast frequency waves on the electroencephalogram (EEG). **N2** is a moderately deep form of sleep, taking up 45% to 55% of the total sleep duration. EEG findings include higher amplitude and slower frequencies than NREM N1 sleep and are marked by expression of spindles and K-complexes (well-defined biphasic waves). **N3** sleep is also known as deep sleep or slow-wave sleep and takes up 15% to

25% of total sleep time. It is characterized by high amplitude waves of low frequency (delta waves). REM sleep follows, and it usually occurs in the second hour after sleep onset. Here, eye movements are rapid, conjugate, and irregular. Low amplitude waves of high frequency characterize the EEG pattern (10).

These regular patterns are interrupted when sleep disturbances occur. Prior studies have tried to pinpoint the physiological correlates of sleep quality. Slow wave sleep, REM percentage, sleep spindles, sleep continuity, K-complexes, total sleep time, amount of night awakenings, and delta NREM EEG activity are among the physiological components postulated. These objective metrics provide information on the physiological mechanisms that occur as a result of a person's sleep experience. They do not, however, make a direct distinction with self-reported sleep quality scores. There are also conflicting results in terms of which objective indicators are most important in self-reported sleep quality assessment (11).

2.3 Epidemiology of poor sleep quality and sleep disorders in HIV

Sleep disruptions can take many forms, with difficulty falling asleep, also known as sleep onset insomnia, and difficulty staying asleep, also known as sleep fragmentation, being the most frequent. Sleep fragmentation can take many forms, including sleep breathing disorders, parasomnias, and sleep movement disorders. Reduced overall sleep quantity may also be a sign of sleep disturbances. These sleep disturbances, in turn, cause daytime sleepiness and impairment in daytime functioning. Given that the daily sleep requirement varies from person to person, sleep quality is more vital than sleep quantity as a measure of sleep sufficiency (10).

Sleep disorders have been shown to occur frequently among HIV patients. In populations without HIV, sleep disturbance has been estimated to range between 13 to 30% (6) while in PLHIV, the predicted range is between 30 to 100% (12). The wide variability could be attributable to the different study methods applied. In a meta-analysis by Wu et al. that included 27 studies assessing a total of 9,246 HIV positive patients, the prevalence of sleep disturbances was 58% (5).

Sleep disturbances in PLHIV are also characterized by difficulty in maintaining sleep, early morning awakening, and difficulties in falling asleep. With regard to sleep architecture, prolonged slow wave sleep, and reduction in REM sleep have been reported (9). Lee et al. conducted a cross-sectional study among 290 adults living with HIV in the USA to characterize the types of sleep problems the patients experienced. In terms of sleep quality, they found that 34% of participants had difficulty falling asleep (prolonged sleep latency), and 56% had severely fragmented sleep.

Total time spent asleep ranged widely from less than 2 hours to more than 11 hours with 45% sleeping for less than 6 hours a night, and 13% sleeping for 8 hours or more. Overall, 65% had poor sleep quality (12).

There is limited data within the African continent on quality of sleep and the sleep disturbances affecting the HIV population. Oshinaike et al. in a study done in Nigeria revealed that 59% of the HIV positive patients had poor sleep quality (13). Desalu et al. also carried out a study in Nigeria using the PSQI to evaluate sleep quality among PLHIV. The occurrence of poor sleep quality was 28.3% (14). In a study conducted in Cameroon, 66.7% of PLHIV reported poor quality of sleep (15).

Numerous comparative studies have been conducted assessing the proportion of sleep disturbances among PLHIV as well as the general public. Low et al. compared the polysomnographic data of HIV positive and negative subjects after controlling for gender, age and the psychiatric diagnoses identified. The findings showed that study subjects who were HIV positive and had insomnia had significantly more prolonged sleep latency, and reduced sleep efficiency by around 8%. They also reported shorter REM sleep duration of between 8 to 10% (9). In another case controlled study conducted in Cameroon comparing the sleep quality of HIV positive and negative individuals using the PSQI, 66.7% of HIV positive study subjects reported poor quality of sleep compared to 11.6% in the control group which included HIV negative population (15).

2.3.1 The burden of poor quality of sleep

The Pittsburgh Sleep Quality Index (PSQI) has been utilized expansively across different settings globally presenting strong validity and reliability in assessing sleep quality of persons living with HIV. Prevalence of poor quality of sleep across these studies has ranged between 40% to 100% based on the PSQI scale (16)(5).

The following table highlights various studies from across the globe that have used the PSQI to assess the prevalence of poor sleep quality in HIV patients.

Table 1: List of PSQI Studies

AUTHOR	STUDY SITE	HIV+ POPULATION SIZE IN STUDY	PREVALENCE OF POOR SLEEP QUALITY
Cruess et al., 2003(17)	North America	57	61.4%
Salahuddin et al., 2009(18)	North America	128	80.5%
Lee et al., 2012(12)	North America	290	65.2%
Crum-Cianflone et al., 2012(19)	North America	193	46.1%
Seay et al., 2013(20)	North America	139	59%
Gamaldo et al., 2013 (21)	North America	25	100%
Oshinaike et al., 2014(13)	Nigeria	300	59.3%
Allavena et al., 2014(22)	France	1354	47%
Faraut et al., 2014(23)	France	640	68%
Gutierrez et al., 2016(24)	North America	176	73%
Huang X et al., 2017(25)	China	4103	43.1%
Redman et al., 2018(26)	South Africa	139	61%
Desalu et al., 2018(14)	Nigeria	602	28.3%
Rodriguez-Estrada et al., 2018(27)	Mexico	367	58.7%

The specific types of sleep disturbances affecting PLHIV have not been entirely distinguished; however, two types have been studied most frequently in association with HIV infection: insomnia, and obstructive sleep apnea.

2.3.2 Insomnia

Insomnia is the most extensively reported sleep disorder in persons with HIV. Earlier studies were mainly based in the laboratory setting, with later studies focusing on subjective tools to assess insomnia and its correlations. Prevalence of insomnia in the general populace is estimated to be 6% to 48% (28). This wide variability is attributed to the variation in case definition and assessment tools used in the different studies. The proportion of insomnia is around 30 percent in the general public. With addition of the daytime symptoms among individuals, the prevalence is

considered to be 10 percent. However when utilizing the DSM-IV guidelines, the prevalence of insomnia is relatively low at 6 percent (28)(29).

Insomnia has also been investigated within the HIV population, though insufficiently. According to a systematic review by Low et al., none of the studies reviewed used the validated clinical diagnostic criteria for insomnia. Other tools such as the PSQI, the Hamilton depression and anxiety scales, and the Wheatly stress profile were employed instead. For instance, Rubinstein et al. reported that 73% of patients with HIV had insomnia based on the PSQI (30). The findings of this systematic review were therefore taken as an estimate of the prevalence of sleep disturbances, rather than of insomnia, ranging from 29% to 97% (31). These findings were similar to those of an earlier systematic review carried out by Reid and Dwyer (7).

Nonetheless, a few studies have utilized specific questionnaires to investigate insomnia in PLHIV. Findings from these studies have indicated that there are higher rates of insomnia among people living with HIV than in the general populace. Faraut et al. made use of a questionnaire tailored to the ICSD-3 and DSM-5 criteria for insomnia to investigate its prevalence in Paris, France. They found that insomnia was prevalent in 50% of PLHIV, compared to a rate of 19% in the general French population, thus the HIV positive population was 2.6 times more likely to have insomnia. This study's strength was its large sample size (640 individuals) and the use of validated questionnaires and diagnostic criteria (23). In a survey conducted by Gutierrez et al., out of 176 HIV seropositive participants, 52% met the diagnosis criteria for insomnia. These patients were assessed using an Insomnia Symptoms Questionnaire (ISQ) whose questions were derived from the DSM-IV criteria for primary insomnia (24).

Adeoti et al., from the African continent, performed a study in Nigeria using the Insomnia Severity Index (ISI), a tool with a diagnostic sensitivity and specificity of 94%. A total of 424 HIV-positive people and a sex- and age-matched control group of 429 HIV-negative people were included in the report. They discovered a prevalence of 49.3 percent and 34.3 percent, respectively, with the difference being statistically significant (32). Insomnia among persons living with HIV has been linked to psychological morbidity, particularly depression and anxiety, antiretroviral therapy, cognitive impairment, and advanced HIV disease stage.

Rubinstein et al. found both anxiety and depressive disorders to be significantly related to insomnia in HIV patients in the USA. Among the HIV patients with insomnia, 40% had depression compared to a rate of 10% among those without insomnia. 65% of HIV patients with insomnia had

anxiety versus 26% of HIV patients without insomnia. Depression was identified as an independent predictor of insomnia (30). In Nigeria, Adeoti et al. also found a link between depression and insomnia (32).

Several antiretroviral drugs are linked with the causation of insomnia (7). These drugs include dolutegravir, raltegravir, efavirenz, nevirapine, and to a much less extent, zidovudine, abacavir, lamivudine, and emtricitabine (33). The two antiretroviral drugs most associated with insomnia are efavirenz and dolutegravir. CNS toxicity has been reported in 40% to 60% of patients on efavirenz, with sleep disturbances comprising nearly half of the cases (34). A meta-analysis of randomized controlled trials showed significantly greater risk for insomnia with dolutegravir than other antiretroviral agents (35).

Rubinstein et al. assessed the cognitive function level to determine if there was any correlation between cognitive function and insomnia. All of the HIV patients in the study with cognitive impairment reported insomnia. In multivariate analysis, they identified cognitive impairment as a statistically significant and independent predictor of insomnia (30).

Insomnia occurs in all stages of HIV disease (30). However, the prevalence is highest in advanced HIV disease. This higher prevalence may be due to central nervous system involvement, or as a symptom of an AIDS-defining illness (7).

2.3.3 Breathing-related sleep disorders

Among PLHIV, it has been observed that obstructive sleep apnea (OSA) is the most prevalent breathing related disorder. Young et al in 1993 estimated the prevalence of sleep-disordered breathing in the general population using polysomnography. It was found that the prevalence of breathing-related sleep disorders defined as Apnea-Hypopnea Index (AHI) of 5 or more was 9% among women and 24% in men. However the study further showed that the prevalence of sleep apnea syndrome (AHI score of 5 or more plus daytime sleepiness) was 2% in women and 4% in men (36).

Senaratna et al. conducted a systematic review in 2017 which found that the global proportion of OSA varied from 9 to 38 percent with clinical OSA (AHI of 15 or more) being between 6 and 17 percent among adults (37). The wide variability was attributed to the difference in parameters used in the various studies, such as the methodology, definition criteria, cut-off levels of indices, and age-grouping. This review's main strengths were the inclusion/exclusion criteria: they included studies from all over the world but only those that were representative of the general population,

and that measured sleep apnea using standardized objective tools, that is polysomnography. An important finding was the absence of any population prevalence study from Africa.

There is limited data on the state of OSA in the African continent, including in the general population's setting. Due to challenges associated with conducting polysomnography as a screening and diagnostic tool, most studies have used validated questionnaires to estimate the prevalence of OSA. Using the Berlin questionnaire, one study in Nigeria found that 19% of the adult population (16% of females and 22% of males) had a high risk for OSA (38). A study conducted among college students in Ethiopia found that 19% were at a high risk of OSA based on the Berlin questionnaire (39). Balkissou et al. used the STOP-BANG questionnaire and found a high risk of OSA in 17.8% of individuals in a semi-urban and rural area of Cameroon (40).

Few studies have investigated for OSA in the HIV population. In 1995 Epstein et al. found OSA in 7% of 134 HIV-positive patients in California, USA (41). In this study, though the initial evaluation included a sleep questionnaire, diagnosis of OSA was confirmed by polysomnography. The prevalence rate was significantly higher than expected for the population under study, as it was relatively young (almost half were in their twenties). Most studies have assessed for the prevalence and risk of OSA among PLHIV by use of questionnaires. More recent studies have found that OSA occurs commonly among people living with HIV. Gutierrez et al. used the STOP-BANG questionnaire and found that 58% of their HIV-positive patient population had moderate to high risk of OSA (24).

The prevalence rate has been shown to be high in both patients on HAART and those not on HAART. Yone et al. set out to investigate the prevalence of high risk of OSA among HIV-positive patients naïve to antiretroviral therapy in Yaoundé, Cameroon. In this cross-sectional study, the STOP-BANG questionnaire was used, and a prevalence of 12.7% (95% CI, 10.2%-15.5%) was found (42). Patil et al. found sleep-disordered breathing to be prevalent in 55.2% of HIV positive men on HAART, and in 53.7% in HIV positive men, not on HAART (43).

It is really uncertain if the HIV population has a higher incidence of OSA than the general population. Patil et al. looked into the relationship between sleep-disordered breathing (SDB), fatigue, HIV infection, and highly active antiretroviral therapy (HAART). They used polysomnography to evaluate SDB. They looked at the prevalence of SDB in three different groups: HIV positive men on HAART, HIV positive men who weren't on HAART, and HIV negative men. SDB was found to be more common in HIV-negative people than HIV-positive

people, with 55.2 percent, 53.7 percent, and 70 percent, respectively, based on an AHI score of 5 events/hour. The prevalence of sleep apnea syndrome was 24.1%, 12.2%, and 26.7% respectively. The finding of a higher prevalence of SDB in the HIV-negative group than the HIV-positive group in this study was not significant (43).

Chen et al. conducted a study in Taiwan to compare OSA incidence among HIV-positive persons with that of HIV-negative matched controls. Findings of this nationwide retrospective cohort study showed that HIV-positive individuals did not have a higher risk of OSA than HIV-negative individuals (44). Kunisaki et al. concluded that HIV-positive persons were three times less likely to be tested for and diagnosed with OSA than HIV-negative persons with prevalence rates of 3.9% and 12.4% respectively. However, they could not ascertain whether this lower prevalence in HIV-infected patients was due to a true decreased likelihood of OSA or decreased screening in this population (45).

Some studies have demonstrated results that are to the contrary. In a study done in Cameroon using the Berlin questionnaire, over 43% of HIV patients were at moderate to high risk of OSA, compared to 14% of HIV negative (p value=0.003, AOR 3.93 95% CI 1.12–13.80) (15).

Certain factors increase the risk of obstructive sleep apnea among persons living with HIV. These include the use of certain antiretroviral drugs, and the effect of the virus itself. The association between ARV drug use and increased risk for OSA is attributed to adverse drug effects, particularly lipodystrophy and weight gain. Certain ARV drugs, such as protease inhibitors are associated with lipodystrophy (46). Lipodystrophy may result in deposition of fat in the neck, and subsequent airway restriction. Deposition and accumulation of fat in the abdomen and thorax may, in turn, increase respiratory effort contributing to the pathogenesis of obstructive sleep apnea (47). Patil et al. found that SDB was significantly more prevalent among HIV-positive men with prior exposure to HAART than those that were HAART-naïve. This was despite a lower body mass index (BMI) range and overall younger age of the persons in the HAART-exposed group (43).

Obesity is a known risk factor for OSA in the general population. It has also been identified as a risk factor in the HIV population (48). Obesity may occur as a result of HIV-associated lipodystrophy. In addition, excess weight gain has been observed among PLHIV who have been switched to an Integrase strand transfer inhibitor (INSTI)-based regimen. However, it is important to note that OSA risk is elevated in HIV patients even in the absence of elevated BMI, obesity, and even in those not on HAART (15)(49). The chronic inflammatory state characteristic of HIV

may be a cause of this increased risk (50). Other risk factors for OSA common to both the general population and the HIV population include advanced age, and male gender (42)(37).

2.4 Mechanisms of poor sleep quality and sleep disturbances in HIV infection

The exact causes and mechanisms explaining sleep disturbances in HIV are not clear. However, there are several postulates:

2.4.1 HIV-specific factors

Though the HIV-specific processes leading to sleep disturbances among PLHIV are poorly understood, the presence of correlates that are specific to the HIV population (such as duration of infection and disease severity) imply the role of several possible mechanisms:

(a)Direct neurotoxic effects of HIV on the central nervous system (CNS).

Though the mechanisms are unclear, it has been postulated that HIV infection of the CNS and the subsequent neuronal damage could predispose to sleep disturbances (31). Soon after primary infection with HIV, CNS invasion occurs via the migration of peripheral macrophages across the blood-brain barrier (BBB) through a "Trojan horse" mechanism (51). CNS infection occurs mainly in macrophages, microglia, and astrocytes. The resulting neurotoxic effects involve (i) the secretion of viral products from infected cells into the extracellular environment, (ii) the mobilization of inflammatory mediators, (iii) the subsequent cycles of direct toxicity and inflammation-causing increasing injury, specifically to dopaminergic and glutamatergic neurons (31).

The major viral proteins recognized as HIV neurotoxins are glycoprotein 120 (gp 120), and trans-activator of transcription (tat) protein. Tat protein is actively secreted by the infected microglia into the extracellular space and CSF, subsequently causing neurotoxicity in two ways. Extracellularly, it modifies neuronal cell homeostasis by altering cell membrane and receptor structures. Intracellularly, it acts on the N methyl-D-aspartate receptor (NMDAR) to augment glutamate transmission. The increased glutamate activity sets off an intracellular cascade resulting in mitochondrial injury and neuronal apoptosis (52)(31). In astrocytes, tat protein stimulates the production of chemokines that induce chemotaxis of inflammatory cells and increases nitric oxide production, impairing the astrocyte's ability to buffer the excitatory glutamate. As a result, extracellular glutamate accumulates resulting in oxidative stress (52)(31).

The HIV surface glycoproteins gp 120 and gp 41 also induce neuronal injury and apoptosis through glutamate excitotoxicity (51). Glutamate excitotoxicity decreases GABA-ergic transmission. GABA (gamma aminobutyric acid) is the brain's primary inhibitory neurotransmitter and it is

responsible for inhibition of the sleep arousal system during onset and maintenance of the sleep state (51).

The notion of viral-mediated neural damage has been backed by various studies, such as one done by Roca C et al. In this study, post-mortem brain analysis was conducted on adults with and without HIV. They found reduced mitochondrial DNA content in those with HIV despite having been virally suppressed (53).

HIV-associated neurotoxic mechanisms can induce significant harm particularly to glutamatergic and dopaminergic neurons, which play significant roles in the sleep-wake function (31). Dopaminergic neurons are essential in signal transmission in various brain areas involved in sleep regulation, affecting both REM sleep and wakefulness. Glutamate is key in promoting cortical, thalamic, and brainstem reticular formation activity. However, glutamate excitotoxicity has been associated with sleep deprivation (54). For these reasons, HIV neurotoxicity can lead to disturbance of sleep patterns. A study supporting this postulation is one done by Opp et al. that linked gp120 and gp41 to the augmentation of fragmented sleep, and the prolongation of NREM sleep in persons with HIV (55).

(b)Role of inflammatory mediators

Inflammatory mediators produced in the course of HIV infection are independent contributors and principal determinants of HIV-related CNS diseases, including sleep disorders (56)(57). Activation of CNS macrophages, microglia and astrocytes occurs either through HIV-1 infiltration or through exposure to secreted viral proteins, particularly gp120 or Tat (51). Once activated, inflammatory mediators secreted by macrophages include Tumor Necrosis Factor-alpha (TNF-), Interleukin-1 (IL-1), and Interleukin-6 (IL-6). These cytokines affect sleep physiology in two ways: Cytokines can cause direct damage to neurons involved in sleep regulation, particularly glutamatergic and dopaminergic neurons. The damage occurs through glutamate-mediated excitotoxicity and release of inflammatory mediators such as reactive oxygen species (ROS), resulting in superoxide-mediated neuronal and microglial apoptosis (51). Furthermore, these inflammatory mediators can also induce microglial phagocytosis of otherwise viable neurons. They also stimulate the expression of adhesion molecules and chemokines which lead to increase in the BBB permeability and further entry of HIV-infected macrophages into the brain (51).

Cytokines can also cause sleep disturbances through the direct modulation of sleep architecture. This can be traced back to the physiological role played by cytokines in normal sleep. TNF-α and

IL-1β have vital sleep-promoting effects. They interact with the hypothalamus-pituitary-adrenal (HPA) axis, thereby enhancing various sleep-regulating hormones (58). These pro-inflammatory cytokines have been shown to enhance slow wave sleep (SWS) and to disrupt REM/NREM sleep cycles in inflammatory conditions (30). A study evaluating the TNF-EEG relationship in HIV patients found that the increased TNF-α level in HIV infection was correlated with higher slow wave sleep in early phases of infection and with sleep fragmentation in later stages of disease (59). Elevated levels of IL-6 and TNF-α have been linked to excessive daytime sleepiness and fatigue such as is encountered in breathing-related sleep disorders, hypersomnia, and insomnia (58).

It is postulated that HIV infection directly contributes to two primary mechanisms of sleep-disordered breathing. One mechanism is the alteration in pharyngeal anatomy linked with HIV disease in early case reports. With the introduction of HAART, HIV-associated adenotonsillar hypertrophy has become rare. Nonetheless, HIV-associated lipodystrophy could result in fat deposition around the pharyngeal airway, increasing airway narrowing/collapse even at lower BMI levels. Another mechanism is the loss of upper airway neuromuscular function. HIV disease is characterized by a chronic inflammatory state with increased and sustained systemic production of cytokines such as IL-1β and TNF-α. These cytokines are thought to act through neural mechanisms to cause myotonic dysfunction of the upper airway musculature (43).

(c)Association of sleep quality with HIV disease stage, immune status, and duration of infection

There is less definitive understanding on the link between sleep quality and other key factors such as HIV disease stage, duration of infection and the patient immune status. A systematic review by Reid and Dwyer in 2005 found that sleep disturbances were frequent in all stages of HIV disease and were not related to severity of illness or categorical stages of HIV infection (7). Other studies have linked poor quality of sleep to longer duration of HIV infection, even with viral suppression (27). A 2014 systematic review found that advanced HIV disease stage, longer duration of illness, and cognitive impairment were significantly associated with sleep disturbances in people living with HIV. However, no correlation was found between sleep disturbances and the immune markers CD4 count and viral load (31). Inversely, a 2017 prospective multi-site study by Womack et al. postulated that viral control may be more essential than CD4+ cell count and specific classes of medications in assessing the sleep disturbance severity for those recently diagnosed with HIV infection (60).

(d)Adverse effects of antiretroviral therapy (ART)

Multiple studies have linked antiretrovirals to sleep disturbances, as well as to various neuropsychiatric syndromes that are associated with sleep disturbances (33). Episodes of psychosis, mood disorders and insomnia have been reported using some nucleoside reverse transcriptase inhibitors (NRTIs) particularly zidovudine, emtricitabine, and abacavir (33). However, other than peripheral neuropathy, NRTI-associated CNS neurotoxicity is uncommon.

Among the non-nucleoside reverse transcriptase inhibitors (NNRTIs), nevirapine and efavirenz have been well studied regarding their neuropsychiatric adverse effects. Nevirapine is linked to insomnia, nightmares, sedation and depression though to a smaller extent(33). Efavirenz is associated with the highest rates of neuropsychiatric side effects among NNRTIs, with psychiatric symptoms reported in 25-40% of patients, and CNS toxicity in general in 40-60% (34). These include sleep disturbances, subjective neurological symptoms, depression, and cognitive impairment. Some studies have shown that most of these efavirenz-associated CNS effects appear early and resolve within a few months. However, in some cases (up to 40% in some reports), these disturbances persist over many years (33)(34).

Integrase inhibitors also cause neuropsychiatric adverse events, such as sleep disturbances (particularly insomnia), depression, anxiety, and psychosis. The highest incidence of neuropsychiatric events reported with the use of integrase inhibitors is attributed to dolutegravir. The rates of sleep disturbances in patients on dolutegravir in SPRING-1, SPRING-2, and SINGLE was 2%, 5%, and 17% respectively. In cohort studies evaluating dolutegravir tolerability, discontinuation incidence due to dolutegravir-associated neuropsychiatric events was in the range of 1.4% to 7.2% (61).

Use of protease inhibitors is associated with the induction of various metabolic processes, including dyslipidemia, peripheral lipodystrophy, central adiposity, and insulin resistance (46). These changes are linked to sleep disorders, particularly sleep-related breathing disorders, and therefore can contribute to the pathogenesis of sleep disturbance in patients with HIV (43)(48).

(e)Presence of physical symptoms

Physical symptoms also contribute to sleep disturbances in persons with HIV. These include symptoms such as pain (including neuropathic pain of chronic inflammation and that of HIV-induced peripheral neuropathy), fatigue, itching, abdominal discomfort, diarrhoea, cough, fever, dyspnea, and night sweats. For instance, chronic pain is common in people with HIV, with a

prevalence of 54% as per a 2014 systematic review (62). A Brazilian study found a high prevalence of poor sleep quality and sleep disorders among HIV patients with neuropathic pain (63). Nokes and Kendrew found that less severity of symptoms correlated with better sleep quality in patients with HIV (64).

2.4.2 Psychological factors

Sleep disruptions are well-known to occur often in a variety of psychiatric disorders. Severe depressive disorder, generalized anxiety disorder, post-traumatic stress disorder, bipolar disorder, schizophrenia, and alcoholism are the psychological conditions most closely linked to sleep disturbances. Insomnia affects between 36-72 percent of patients with alcoholism, and sleep disturbances affect over 90 percent of patients with depression and over 50 percent of patients with anxiety (65). This is in keeping with findings from various studies which have reported a significant association between sleep disturbance in HIV and psychiatric disorders, particularly depression and anxiety(25)(32)(66). Ng'ang'a et al. found the prevalence of depression and anxiety among HIV patients attending the KNH Comprehensive Care Centre to be 47.25% and 22.75%, respectively (67).

2.4.3 Sociodemographic factors

Older age is strongly associated with poorer sleep quality, and the association is independent of underlying chronic conditions (68). With this in mind, it is vital to note that HIV infection has accelerated the aging process. This was evidenced by Horvath et al., who found that DNA methylation, a marker of epigenetic aging, was increased in persons with HIV (69). This could explain the higher prevalence of poor sleep quality in younger age groups of people living with HIV.

Studies conducted in the general population suggest that sleep disturbances are more likely to be reported by women than by men. A similar trend is seen with findings of many studies done in the HIV population. The same was inferred by Jie Wu et al., in a meta-analysis of the prevalence and moderators of sleep disturbances in HIV-infected people (5).

Alcohol use, cigarette smoking and use of illicit drugs are known to cause sleep disturbances. However, their effect on HIV has been considered only in very few studies (22)(27). A meta-analysis on the prevalence and correlations of insomnia in persons with HIV done by Reid et al. found that most studies did not assess these factors. In addition, others used them as part of their exclusion criteria (7).

Studies have shown that married people report better sleep quality than those that are single, which has been attributed to the positive psychological impact of companionship. The same reason applies for the better quality of sleep reported by patients with good social support (22)(25).Studies have linked unemployment and low economic status to poorer quality of sleep. This is attributed to the associated financial and psychological stress caused (22).

2.5 Implications of poor quality of sleep and sleep disorders on persons with HIV

2.5.1 Increased risk of metabolic and cardiovascular diseases

HIV positive adults have a 1.6 to 2 times greater risk of cardiovascular disease than HIV negative adults (70). Lipodystrophy, diabetes mellitus, and hyperlipidemia, all of which are related to cardiovascular disease, are common in HIV patients, including those on HAART (71). The increased risk among persons living with HIV has been attributed to various factors such as the HIV virus itself, the effect of chronic inflammation, and antiretroviral therapy. HIV infection is characterized by sustained immune activation and chronic inflammation even after viral suppression has been achieved using HAART (72). In HIV disease, this chronic inflammatory state has been shown to be a predictor of cardiovascular morbidity and mortality. An analysis of the incidence of cardiovascular disease outcomes in HIV patients showed that HIV patients had higher rates of IL-6 and D-dimers, which were linked to a higher risk of cardiovascular disease-related mortality (73).

Sleep disturbances contribute further to this cardiovascular and metabolic disease risk. Insufficient sleep period and poor sleep quality were established as significant and independent risk factors for the development of cardio-metabolic diseases such as hypertension, obesity, type 2 diabetes mellitus, and cardiovascular disease such as coronary heart disease, as well as their related adverse events, in a meta-analysis by Kwok et al. of 60 studies with over 3 million participants. Furthermore, a longer sleep period was linked to a higher risk of all-cause mortality (74). Evidence has shown that poor sleep quality significantly increases the risk of metabolic disorders (75). A study done in Kenya by Sokwalla et al. demonstrated a high prevalence of poor sleep quality in patients with type 2 diabetes mellitus (76).

Several mechanisms postulate the relationship between sleep disturbance and increased risk of cardio-metabolic disease in persons with HIV. Poor sleep quality has been linked to inflammation, and in HIV infection, this acts to propagate the chronic inflammatory state. Systemic inflammation in turn promotes insulin resistance and atherosclerosis (75). There is increased production of

cytokines such as IL- 1β, IL-6, TNF-α and C-reactive protein in sleep disorders such as insomnia and OSA. These cytokines increase the risk of cardiovascular disease and associated events among people living with HIV (4). Brigham et al. discovered that markers of systemic inflammation (TNF-α and IL-6) were higher in HIV positive patients with obstructive sleep apnea than in HIV negative patients with obstructive sleep apnea. They also discovered a connection between obstructive sleep apnea and high TNF-α, which was independent of HIV viral load and CD4 T cell count (77).

Sleep disturbances alter the normal circadian rhythms, which results in alteration of various physiological systems such as the leptin and ghrelin system. Sleep disruption induces leptin suppression and ghrelin stimulation. This results in increased appetite, decreased satiety, thus increased intake of energy and storage of fat. Weight gain and ultimately obesity follow, significantly increasing the risk of type 2 diabetes by stimulating insulin resistance (75)(78). Some studies have shown elevated levels of leptin with sleep restriction, but still with decreased satiety, suggesting an element of leptin resistance (75). Sleep disturbances also trigger the reduction of the basal metabolic rate and insulin secretion, thus promoting hyperglycemia (78).

The normal HPA axis rhythm is characterized by higher hormone levels early in the morning, declining levels during the day with prolonged low levels around midnight, followed by a rise in the latter part of the night. By altering this circadian-regulated rhythm, sleep disturbances may lead to hyperactivation of the HPA axis. This hyperactivated state has also been attributed to the intermittent hypoxia that occurs in obstructive sleep apnea. HPA axis hyperactivation in turn stimulates increased cortisol production and increased sympathetic nervous system activity. High levels of cortisol, norepinephrine and epinephrine promote insulin resistance, hyperglycemia, and accumulation of visceral fat leading to diabetes and obesity (78).

Sleep pathways and autonomic pathways have been shown to be related, not only through their neuroanatomical proximity, but also through direct circuit connections. With the transition from wakefulness to normal sleep, parasympathetic vagal tone escalates while the sympathetic tone reduces. Sleep disruption can trigger bursts of sympathetic activity therefore higher nighttime heart rate and blood pressure. A similar sympathetic surge response occurs with the intermittent but repetitive hypoxia of obstructive sleep apnea. With frequent sleep disruption, these surges of sympathetic activity can persist to the wakeful state during the day, leading to hypertension (79).

A possible explanation for this "carryover effect" is that short duration of sleep markedly reduces the period known to be the restorative stage of sleep, that is, the slow-wave sleep (78).

Formation of coronary calcifications has been significantly linked to short sleep duration (78). Poor sleep quality results in fatigue and excessive daytime sleepiness, which inadvertently increase physical inactivity, a known leading risk factor for cardiovascular disease.

Research has shown that sleep restriction can alter expression of genes associated with oxidative stress and metabolism, therefore influencing metabolic and cardiovascular function at the molecular level (78).

2.5.2 Development of psychiatric disorders

Sleep disturbance can lead to the development of psychiatric disorders particularly anxiety and depression. Breslau et al. found that prior insomnia substantially predicted subsequent onset of major depressive disorder (80). A study by Neckelmann et al. identified insomnia as a risk factor for the onset of anxiety disorders (81).

Anxiety and depression are in turn linked to the development of sleep disturbance hence a bidirectional cause-effect relationship is suggested. This bidirectional relationship confers potential for further perpetuation of psychiatric illness and/or sleep disturbance (82). In persons with HIV, psychiatric conditions such as depression have been shown to contribute to poorer health and treatment outcomes. Depression contributes to non-adherence. A systemic review of sub-Saharan studies on the association between depression and ART adherence found that in those with depression, the chance of attaining good adherence was 55% lower than in those without depression (83). Several studies have also demonstrated a connection between anxiety and ART non-adherence (84).

2.5.3 Cognitive Impairment

Studies conducted among persons living with HIV have demonstrated that poor quality of sleep significantly undermines cognitive functioning (85). Impairment of cognitive functions such as memory, concentration, and decision-making increases the risk of ART non-adherence (86).

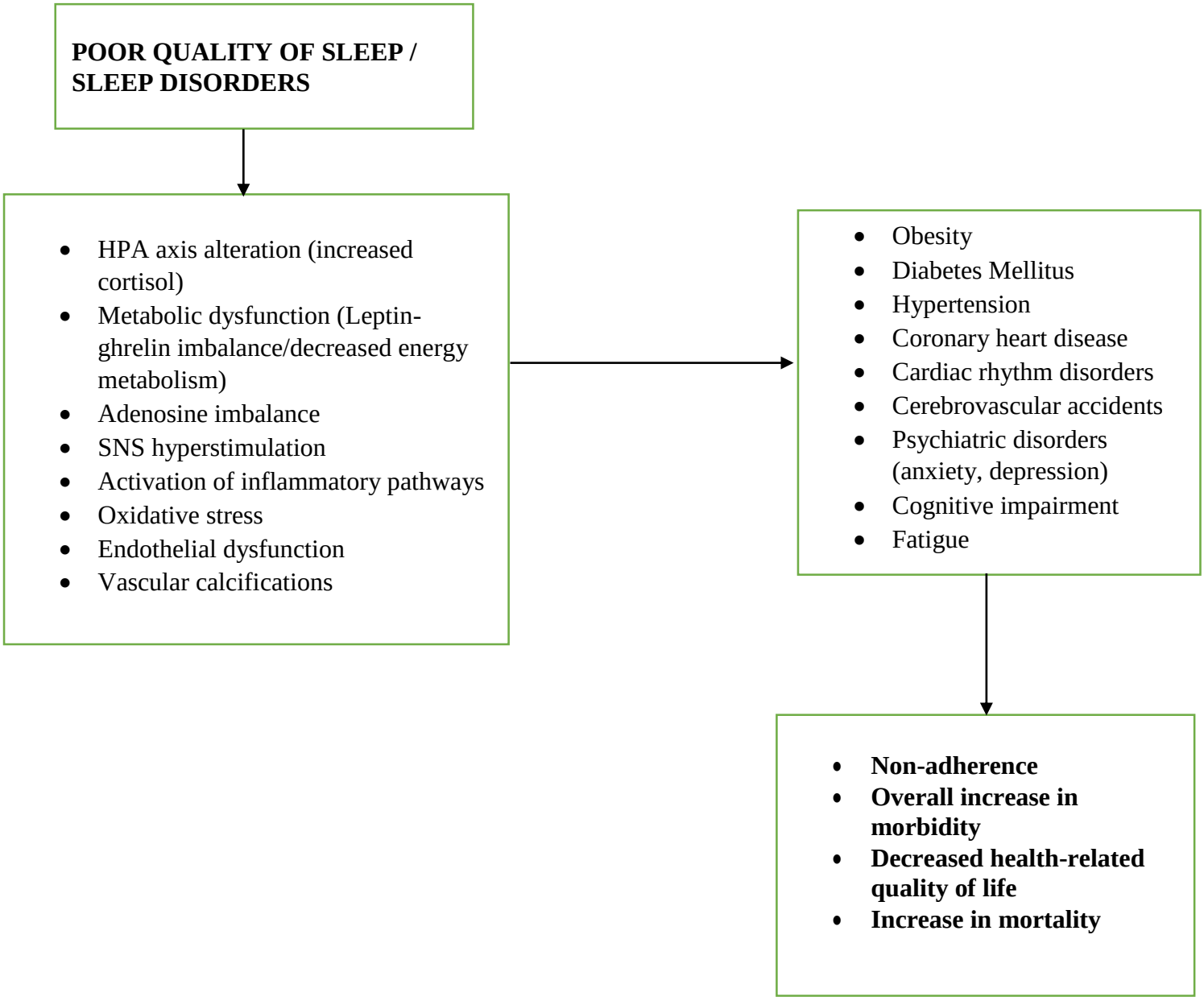
2.5.4 Poor adherence

Poor quality of sleep in patients with HIV may result in poor adherence to antiretroviral therapy. This relationship may be explained by the presence of psychiatric conditions such as depression, or by cognitive impairment resulting from sleep disturbance (87)(88). Poor adherence in turn contributes to treatment failure, drug resistance and disease progression.

2.5.5 Impact on quality of life

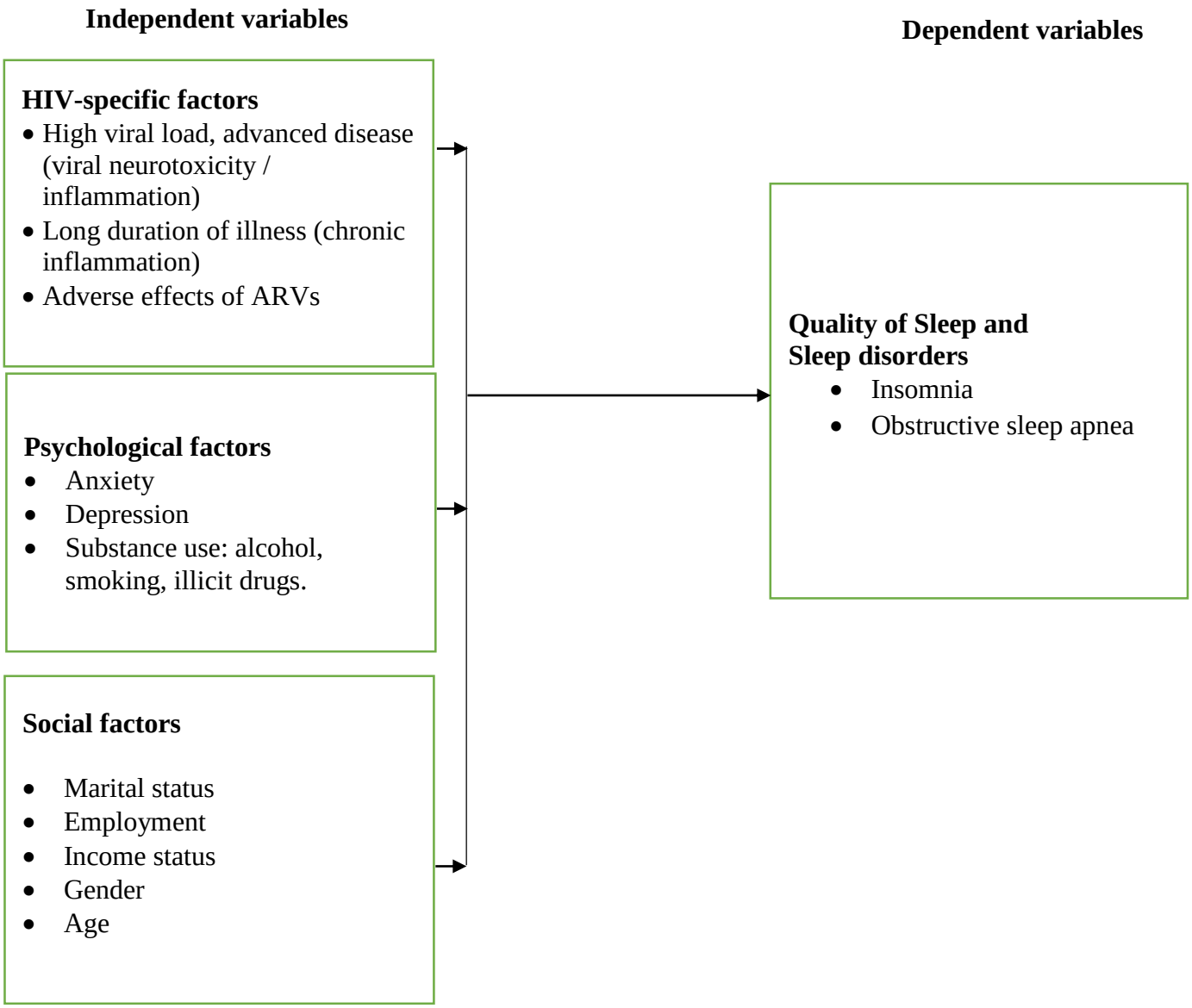
Health-related quality of life is a concept with multiple dimensions. It refers to the impact of one's health status on various domains related to their overall physical, mental, emotional, social, and behavioural wellbeing and function. Poor sleep quality in persons with HIV is independently associated with a low quality of life (89).

Figure 1:Implications of sleep disturbances



2.6 Conceptual framework

Figure 2: Conceptual Framework

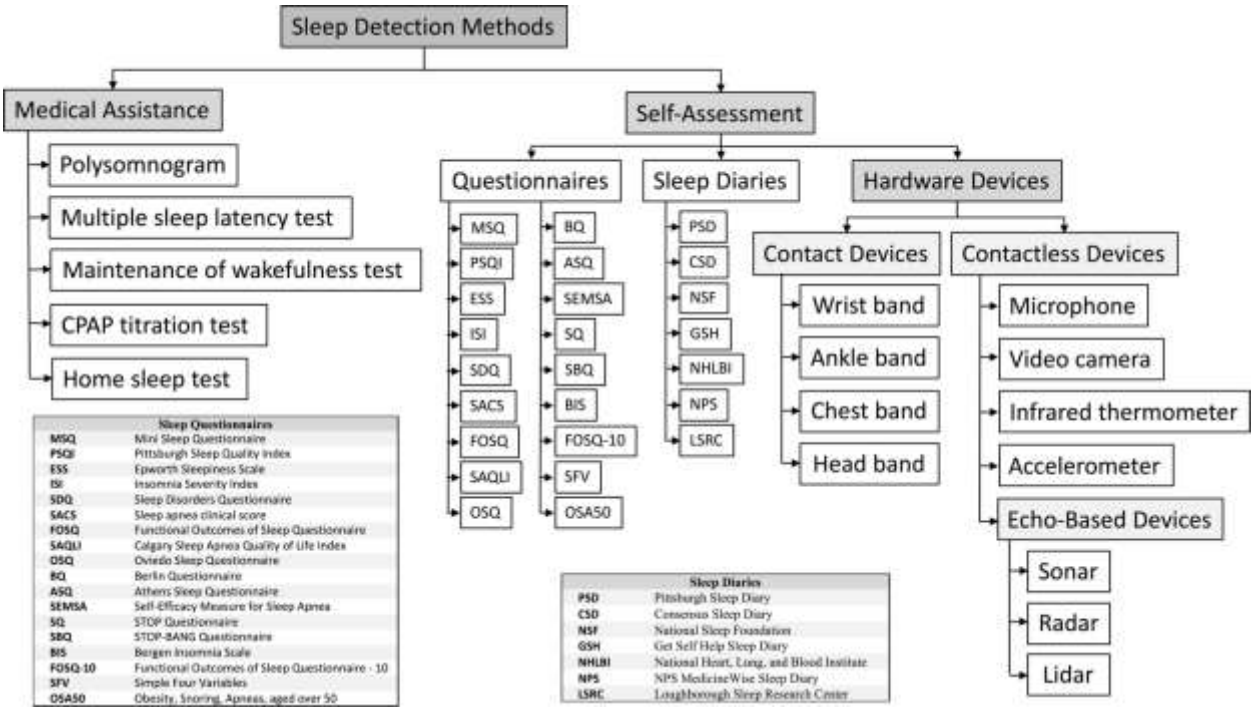


2.7 Assessing sleep quality and screening for sleep disorders

There are various clinical tools used globally for the screening, evaluation, and diagnosis of sleep disorders. These tools can be broadly grouped into two: medical assistance methods and self-assessment methods. The medical assistance methods are those that require significant clinical intervention so as to be undertaken, such as requiring a lab setting for part or the whole of the assessment. These include polysomnography, the maintenance of wakefulness test (MWT), the multiple sleep latency test (MSLT), the CPAP titration test and the home sleep test.

The self-assessment methods include both subjective and objective methods. The subjective methods include clinical interviews, use of sleep diaries, and self-report questionnaires, whereas objective methods involve the use of devices, such as actigraphy. The methods most commonly used for sleep assessment are described below.

Figure 3:Taxonomy of sleep detection methods



Taxonomy of sleep detection methods (90).

2.7.1 Clinical Interviews

The use of clinical history as a diagnostic tool for the diagnosis of sleep disorders requires thorough inquiry of the symptoms, associated factors, chronicity, medical interventions, past medical history, and life events, among other details to come to a diagnosis. This is preferentially guided by an interview format of assessment, either structured or semi-structured. One such structured interview tool is the Duke Structured Interview for Sleep Disorders. This interview tool assesses the symptoms of sleep disorders as per criteria found in the DSM and ICSD. The tool consists of about 8 pages with 20 to 51 questions. Other similar interview tools are the Insomnia Interview Scale and the Structured Interview for Sleep Disorders. The advantage of using such interview tools is that they allow for a thorough assessment of the sleep disturbance. They also give provision for in-depth analysis of functional status and formation of appropriate differential diagnosis. The limiting factor though is that their application requires above-average knowledge of sleep disorders in their variety. Moreover, the information used is largely subjective thus reducing accuracy in the diagnostic formulation (90).

2.7.2 Sleep Diary

This method of assessment requires the patient to input information about their sleep patterns in a journal daily. The information captured includes the time of going to bed, the time at which they awake, sleep-onset latency, number of awakenings and their respective durations, duration of sleep, any daytime sleep, total time spent in bed, as well as sleep efficiency. After a period of at least two weeks of daily entries, the sleep diary can then be evaluated by a clinician. The tool has the advantage of enabling the clinician to evaluate the nature of the sleep disturbance in detail, by easily tracking nocturnal variability as well as any perpetuating factors. It also provides the element of ecological validity because the evaluation occurs while the patient is in their usual or natural environment, therefore better characterization of the sleep disturbance. The patient can also be studied for a longer time period as assessment does not interfere with their daily activities. However, its diagnostic accuracy is highly dependent on the patient's adherence (90).

2.7.3 Actigraphy

Actigraphy refers to the measurement of a person's cycles of activity and rest using a device (an actigraph) that continually senses and records movement while worn on the wrist. After that the recordings are analyzed via computer programs and are used to determine a person's sleep patterns. This instrument can also be used to assess the effectiveness of different therapeutic interventions used for various sleep disorders. Actigraphy has the advantage of allowing assessment of the

patient in their natural environment since the device can be worn continuously and is non-invasive. In addition, as it is objective, data obtained is more accurate than that of self-reported tools. However, it does not provide information on sleep architecture such as identification of the stages of sleep. Its use is also limited in patients with sleep-associated movement disorders (91).

2.7.4 Polysomnography (PSG)

This refers to the electrophysiological monitoring of sleep through the night by use of electromyography (EMG), electro-oculography (EOG), electroencephalography (EEG), pulse oximetry, and airflow assessment using respiratory monitors. PSG is considered the gold standard for the diagnosis of sleep-disordered breathing and is useful for the assessment and adjustment of treatment such as in titration of positive airway pressure. It is also very useful for the evaluation of sleep-associated movement disorders, among other sleep disorders. It provides an objective assessment of sleep disorders and the most detailed information on sleep architecture. A drawback to the use of polysomnography is that it is mostly done in a laboratory setting, which creates an aspect of inconvenience. Besides, since the patient is not in their usual environment, there is possibility of the findings being an inaccurate representation of the patient's usual sleeping patterns. It is also expensive to undertake, not widely available, is labour-intensive, and requires high expertise. It is also less informative for some disorders such as behavioural insomnia and daytime sleepiness (92).

2.7.5 Multiple Sleep Latency Test and Maintenance of Wakefulness Test

These two tests are both methods used for the evaluation of excessive daytime sleepiness (as occurs in narcolepsy and idiopathic hypersomnia). They are carried out in a laboratory setting, and readings are obtained using electrodes for EEG, EOG, EMG and ECG measurements. These methods are however limited in use in the diagnosis of other sleep disorders. They are also limited to the lab setting, are cumbersome to conduct, and very time-consuming as each test takes a complete day to be done (90).

2.7.6 Sleep Questionnaires

Sleep questionnaires form a key part of the preliminary assessment of sleep. The reason for this is that they take a short time to conduct, are very inexpensive, easy to carry out, and also bring out the patient's own perspective on the quality of their sleep. However, this same subjective nature is the main limitation of sleep questionnaires, as the findings are subject to bias. However, despite their subjectivity, questionnaires have been validated through various studies and found to be highly specific and sensitive. Their sensitivity is often above 90%, with specificity ranging between 50% and 96% (90).

The following table lists the most comprehensive sleep questionnaires used in the last 30 years as compiled by Ibáñez et al. in a 2018 survey (90):

Table 2:Types of sleep questionnaires

Sleep Questionnaire	**Measure / Indication**
Mini Sleep Questionnaire (MSQ)	Insomnia and hypersomnia
Pittsburgh Sleep Quality Index (PSQI)	Sleep quality and patterns of sleep in adults
Epworth Sleepiness Scale (ESS)	Level of daytime sleepiness. Average sleep propensity in daily life
Insomnia Severity Index (ISI)	Nature, severity, and impact of insomnia. Treatment response in adults.
Athens Insomnia Scale	Insomnia
Sleep Disorders Questionnaire (SDQ)	Sleep disturbance and usual sleep habits during the last month only.
Sleep Apnea Clinical Score (SACS)	Sleep apnea.
Functional Outcomes of Sleep Questionnaire (FOSQ)	Impact of excessive sleepiness on daily life.
Calgary Sleep Apnea Quality of Life Index (SAQLI)	Quality of life associated with sleep apnea.
Oviedo Sleep Questionnaire (OSQ)	Insomnia and hypersomnia in the last month.
Berlin Questionnaire (BQ)	Sleep apnea.
Athens Sleep Questionnaire (ASQ)	Sleep quality.
Self-Efficacy Measure for Sleep Apnea (SEMSA)	Sleep apnea.
STOP Questionnaire (SQ)	Sleep apnea.
STOP-BANG Questionnaire (SBQ)	Sleep apnea.
Bergen Insomnia Scale (BIS)	Sleep quality.
Functional Outcomes of Sleep Questionnaire – 10 (FOSQ-10)	Impact of excessive sleepiness on daily life.
Simple Four Variables (SFV)	Sleep apnea.
Obesity, Snoring, Apneas, aged over 50 (OSA50)	Sleep apnea.

2.8 Study justification

HIV positive adults have about 2 times higher risk of cardiovascular disease than HIV negative adults, even after controlling for ART use, traditional risk factors, and HIV viral load. Poor sleep quality and sleep disorders, which are significant independent contributors to increased morbidity and mortality, are more prevalent among PLHIV relative to the general population. Sleep disorders further increase the risk of cardiovascular disease in PLHIV. Poor sleep quality is known to impact health-related quality of life. Obstructive sleep apnea is a known risk factor for cardiometabolic diseases and chronic inflammation, both of which disproportionately impact patients with HIV. Sleep disorders are largely underdiagnosed and untreated. The burden of obstructive sleep apnea and poor quality of sleep among HIV patients in Kenya is not known. Through this study, we hope to generate preliminary data on the burden of poor sleep quality and risk for obstructive sleep apnea with the goal of increasing awareness among patients and healthcare providers.

2.9 Research question

What is the quality of sleep and risk for obstructive sleep apnea in adult patients with Human Immunodeficiency Virus attending the HIV clinic at the Kenyatta National Hospital?

2.10 Broad objective

To determine the quality of sleep and risk for obstructive sleep apnea in adults with HIV infection at the Kenyatta National Hospital.

2.10.1 Specific objectives:

1. To determine the quality of sleep of adult patients with HIV using the Pittsburgh Sleep Quality Index.
2. To determine the risk for obstructive sleep apnea in adult patients with HIV using the STOP-BANG questionnaire.

2.10.2 Secondary objectives:

1. To determine the association between quality of sleep and depression in adult patients with HIV attending the HIV clinic at KNH.
2. To determine the association between quality of sleep and anxiety in adult patients with HIV attending the HIV clinic at KNH.
3. To assess factors associated with poor sleep quality and high risk for obstructive sleep apnea.

3 CHAPTER THREE: METHODOLOGY

3.1 Study design

This was a hospital-based cross-sectional study.

3.2 Study population

The study population consisted of adult HIV patients attending the Comprehensive Care Centre (CCC) of Kenyatta National Hospital. Individuals who work night shifts, pregnant women and those on psychoactive drugs were excluded.

3.3 Study site

The study was carried out at the Comprehensive Care Centre (CCC) of Kenyatta National Hospital (KNH) in Nairobi, Kenya. Kenyatta National Hospital is the country's major teaching and referral hospital, as well as one of the most central health facilities for residents of Nairobi and its environs. The CCC offers a whole range of HIV care including Nutrition, Counseling, Pharmaceutical Care, PMTCT, PrEP, Laboratory diagnosis and monitoring of both adults and children. Patient information is stored in an electronic medical record known as the KenyaEMR. The data stored includes information such as date of diagnosis, date of enrollment into care, date of initiation on ART, previous and current regimen, previous and current CD4 count and viral load, current WHO stage, past medical history, family history and social history. The data is secured and accessible only to authorized persons. The clinic runs from 8a.m to 4p.m from Monday to Friday. About 7000 adults are enrolled at the clinic with about 60 adult patients attending the clinic per day.

3.4 Case definition

Adult HIV seropositive patients who attended the Comprehensive Care Centre (CCC) of Kenyatta National Hospital.

3.5 Participant selection

3.5.1 Inclusion criteria:

1) HIV seropositive individuals above the age of 18 years.
2) Those willing to participate by giving consent to the study.

3.5.2 Exclusion criteria:

1) Individuals on night shift work (whereby at least half of the working hours are between 11pm and 8am).
2) Pregnant women and women in the postpartum period.
3) Individuals on psychoactive medication such as anxiolytics, antidepressants, mood stabilizers, antipsychotics, or antiepileptic drugs.

3.6 Sample size

We used a single population to estimate the proportion of HIV positive patients with the outcome of interest. Sample size was calculated using Fisher's formula as follows:

$$n = \frac{Z^2 P(1-P)}{d^2}$$

Where:

n – minimum required sample size

Z – standard normal for a 2-sided test at 95% confidence interval (CI) = 1.96

P – Estimated proportion of HIV patients with outcome of interest

d – margin of error of estimation = 5%

Substituting into the formula,

Outcome of interest	**Proportion (P)**	**Sample size (n)**
Poor sleep quality	28.3% (Desalu et al., 2018)	312
High risk of OSA	12.7% (Yone et al., 2020)	170

The minimum sample size required was **312** HIV positive patients to estimate the outcomes within 5% level of precision.

3.7 Sampling procedure

Random sampling technique was used to select patients to participate in the study. The investigator generated a list of all the adult patients on follow up at the clinic. This list formed the sampling frame to select patients into the study. The sampling frame was serialized and patients selected using random numbers generated from Microsoft Excel. Patients whose scheduled clinic appointment was not within the study period were called and their transport fully catered for. Recruitment into the study was done until the desired sample size was achieved.

3.8 Recruitment and consenting procedure

HIV positive patients who were sampled randomly were screened to investigate whether they meet the inclusion criteria by the principal investigator with the help of research assistant. This was done using a pre-developed study proforma (*appendix 2*). The eligible patients were then taken through the consenting process. This involved disclosing full information about the study. Benefits and risks of the study were fully explained to the patients before they could consent as shown in consent form (*appendix 3*). The patients were given an opportunity to participate in the study

voluntarily. Those that understood and consented to the study were recruited. Recruitment was conducted from Monday to Friday (8am to 4pm).

3.9 Data collection tools and procedures

3.9.1 Data collection tools

- A study proforma
- The Pittsburg Sleep Quality Index (PSQI) questionnaire
- The STOP-BANG questionnaire (SBQ).
- The Patient Health Questionnaire 9 (PHQ-9)
- The Generalized Anxiety Disorder 7 (GAD-7)
- A standard digital weighing scale calibrated to the nearest 100 grams
- A standard stadiometer calibrated to the nearest 1 centimeter.
- A measuring tape calibrated to the nearest 1 millimeter.

3.9.2 Data collection procedures

3.9.2.1 Study Proforma

The participants' socio-demographic data (gender, age, education level, employment status, and marital status) was obtained through patient interviews using the study proforma. The study proforma was also used to record data abstracted from the patient's medical records. The data abstracted included viral load, CD4 count, disease characteristics and presence of any comorbidities. The data recording on the study proforma was proceeded by administration of the four validated study questionnaires as discussed below.

3.9.2.2 Pittsburgh Sleep Quality Index (PSQI)

The PSQI questionnaire was administered to the study participants to determine sleep quality. It is a tool that includes 19 items that measure seven key areas of sleep quality. The items were measured on a Likert scale that ranges from 0 to 3, where 3 is the worst outcome. The index score was calculated by summing up the component scores. The PSQI has been validated in several population and patient groups including among PLHIV and it has been translated in over 56 languages. A score >5 defines poor quality sleep. This was based on validated scale which revealed 89.6 percent sensitivity and 86.5% specificity (93).

3.9.2.3 Stop-Bang Questionnaire (SBQ)

The STOP-Bang questionnaire was used to screen for obstructive sleep apnea (OSA). The scores for SBQ range from 0 to 8. A stop-bang score of 3 or more predicts moderate to severe OSA

(apnea-hypopnea index [AHI] > 15) and severe OSA (AHI > 30) with a sensitivity of 93% and 100% respectively, and specificity of 90% and 100% (94). Comparable diagnostic by Chiu et al. established that found the SBQ to be the more precise tool for identifying mild, moderate, and severe OSA (95). Moreover, Bosompra et al. assessed the validity of sleep questionnaires, and found the SBQ to have better sensitivity than the BQ and the ESS in people living with HIV (96).

3.9.2.4 Patient Health Questionnaire (PHQ-9)

The PHQ-9 was used to screen for depression. It is a self-administered questionnaire consisting of 9 items graded on a four-point Likert scale (0–3). Using this tool, a total score of five (5) or more indicated presence of depression. This tool has been validated in various populations and patient groups, including among persons living with HIV. The PHQ-9 was found to have high validity and reliability among people living with HIV in a study conducted in Western Kenya (97).

3.9.2.5 Generalized Anxiety Disorders Scale (GAD-7)

The GAD-7 was administered to study participants to test for anxiety. It is a self-administered questionnaire consisting of seven-items each graded on a four-point Likert scale (0-3). A total score of 5 or more indicated presence of anxiety. The GAD-7 has been validated in various population groups, including among people living with HIV (98). It has also been evaluated in the Kenyan context and found to be a valid and reliable screening tool for anxiety among adults with HIV (99).

3.10 Definition of terms

1. **Body mass index**: This was calculated and expressed in kg/m2.
2. **Neck circumference**: This was calculated using a measuring tape.
3. **Poor quality of sleep**: A global PSQI score of >5 indicated poor sleep quality.
4. **Low risk for OSA**: This was defined by a STOP-BANG score of <3.
5. **High risk for OSA:** This was defined by a STOP-BANG score of 5-8, or:

   a score of ≥2 + male gender,
   or a score of ≥2 + BMI > 35kg/m^2
   or a score of ≥2 of 4 STOP questions + neck circumference 16 inches / 40cm.

6. **Depression:** This was defined by a score of ≥5 on the PHQ-9.
7. **Anxiety:** This was defined by a score of ≥5 on the GAD-7.

3.11 Quality assurance

All the four questionnaires are validated and have been used widely among people living with HIV. The questionnaires were translated into Kiswahili for ease of patients understanding. The study assistants were adequately trained by the principal investigator (PI) on the procedures pertaining to case recruitment and data collection before the onset of the study and therefore were well acquainted with use of all the research tools. The PI conducted a data verification process at the end of each day of data collection to help in minimizing errors thus ensuring the provision of reliable data. The PI had overall responsibility and oversight of the study.

3.12 Data management and analysis

To eliminate any chance of double data entry, each proforma was serialized with a unique identifier. Data collection forms and the signed consent forms were stored in a secure lockable cabinet accessible only to the principal investigator.

Data was entered and managed in epi-data version 3.1. Data was exported to SPSS for cleaning and analysis. Normally distributed continuous data was analyzed using means (SD) and median (IQR) for skewed data. Categorical data was analyzed and presented as frequencies and percentages.

The percentages of sleep quality and obstructive sleep apnea risk were calculated and displayed with a 95% confidence range. In order to compare medians, the Mann Whitney U test was used whereas the student's t test was used to compare means. Bivariate analysis employed the student t

test, Fisher's exact, and Pearson's chi square. To account for confounding effects, multivariate analysis was used to independent variables that were found to be significantly linked with both obstructive sleep apnea and the quality of one's sleep at the bivariate level. A logistic regression model was used to evaluate parameters related to sleep quality and obstructive sleep apnea in HIV positive patients while correcting for confounding variables. At a significance level of 5%, all statistical tests were conducted. The findings of the study were presented using tables and graphs.

3.13 Ethical Considerations

The study sought approval from the KNH-UoN Ethics and Review Committee. In addition, the study sought permission from Kenyatta National Hospital administration to allow data collection within the institution. The eligible patients were only recruited after consent. The consent included the following:

- The purpose of the study was explained to the subjects, with clear elaboration of the various study tools and procedures.
- The subjects were assured that their participation in the study would be voluntary, and that no medical service would be denied should they decline to participate.
- The subjects were assured of confidentiality. Patients' confidentiality was maintained by assigning codes to the questionnaires. The interviews were conducted in a private area within the clinic so as to ensure that the participants felt comfortable answering personal questions.

The participants answered the questions at will without any coercion and were assured of their freedom to exit the study once they felt their personal space was being intruded.

With the ongoing covid-19 pandemic, certain measures were taken to prevent infection and spread. These measures included the following:

- Screening of the participants was done by the principal investigator for symptoms suggestive of covid-19 infection. Participants with suggestive symptoms were excluded.
- The study assistants were screened on a daily basis by the principal investigator for symptoms suggestive of covid-19 infection.
- The principal investigator provided hand sanitizers for use at the study site. The participants were required to sanitize their hands upon arrival. The principal investigator

and study assistants ensured to sanitize their hands before and after interacting with each participant.

- Tape measures were decontaminated after each use using alcohol-based sanitizer.
- Social distancing was enforced and maintained in the waiting area and during interactions with study participants.
- The principal investigator availed 3-ply masks to the study assistants and study participants. The principal investigator, study assistants, and study participants were required to remain masked at all times.

4 CHAPTER FOUR: RESULTS

4.1 Introduction

The study sought to determine the quality of sleep and risk of obstructive sleep apnea in adults with HIV infection at the Kenyatta National Hospital. A total of 312 HIV positive adults attending clinic at Kenyatta National hospital were targeted. All the participants completely filled the study questionnaires and were all included in the analysis representing a 100% response rate.

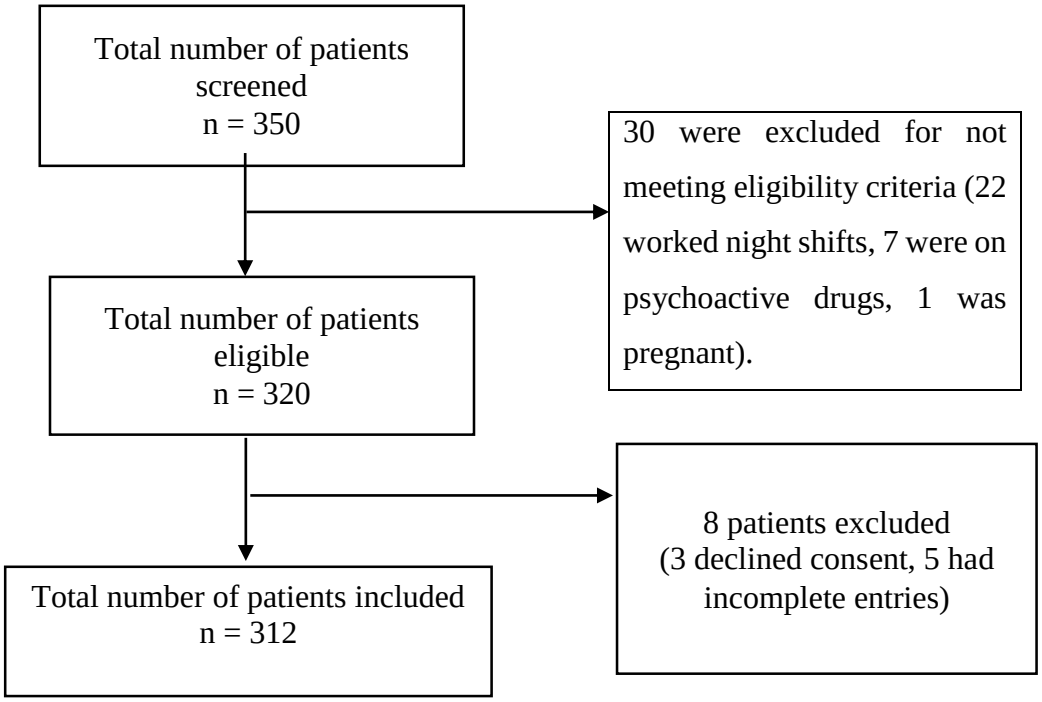


Figure 4: Study Flow chart

4.2 Descriptive analysis of the findings

4.2.1 Age distribution of the respondents

The visual representation of age as shown follows almost a normal distribution with most values lying closer to the mean which was 44.96 (SD =10.7) as shown in Figure 5.

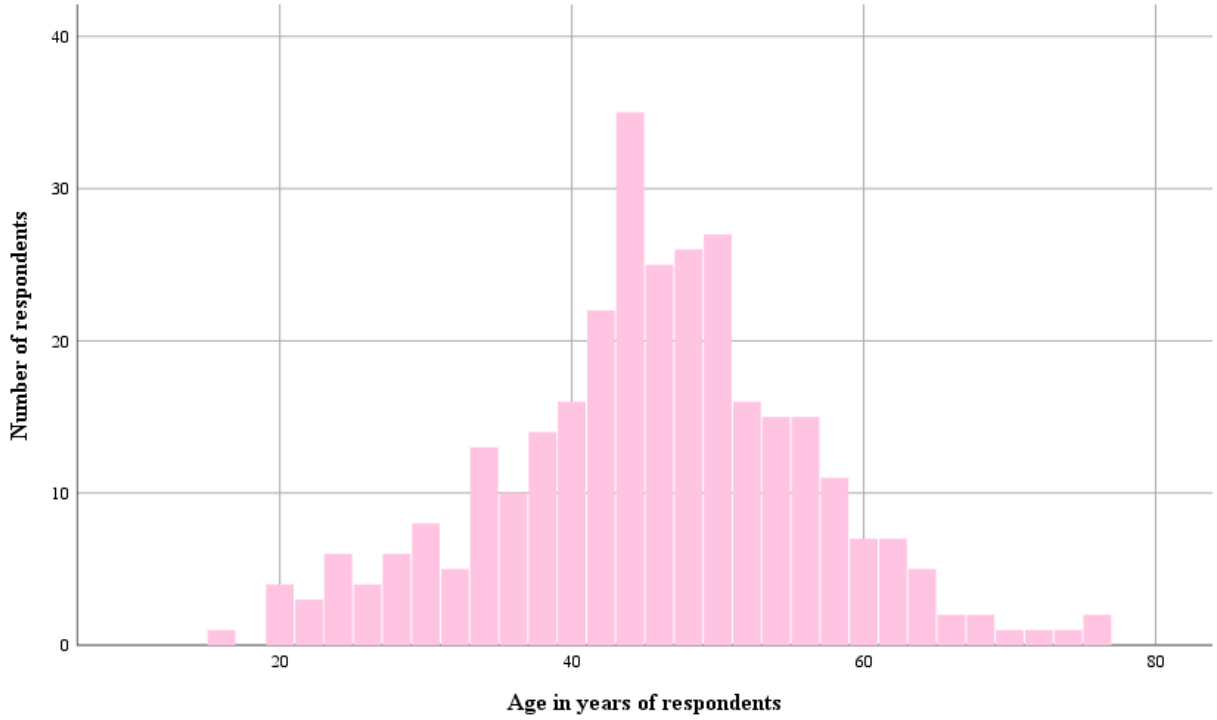


Figure 5: Age distribution in years

4.2.2 Demographic characteristics of HIV positive patients attending clinic at Kenyatta National Hospital

More than half, 57.4% (179) were female, and the average age was 44.9 (SD = 10.7) years. 39.4% (123) of the respondents had attained secondary level education. 49% (153) of the respondents had partners. Majority of the respondents, that is, 81.7% (255) resided in urban areas. 65.7% (205) were formally employed with an average income of Ksh.20,112. 21.5% (67) of the respondents used alcohol, 5.8% (18) used cigarettes, 1.6% (5) used Khat while 1.9% (6) used recreational drugs such as marijuana as shown in Table 3.

Table 3:Demographic characteristics of HIV positive patients attending clinic at Kenyatta National Hospital

Demographic factors	**Frequency**	**Percent**
Gender		
Male	133	42.6
Female	179	57.4
Age (Median (IQR) years	45(39 -52)	
Level of education		
None at all	10	3.2
Primary	72	23.1
Secondary	123	39.4
Tertiary	107	34.3
Marital status		
Single	96	30.8
Married	153	49.0
Divorced	8	2.6
Widowed	30	9.6
Separated	25	8.0
Residence		
Urban	255	81.7
Rural	57	18.3
Employment status		
Formally Employed	205	65.7
Not employed	107	34.3
Monthly income (Median (IQR) Ksh.	20,000(10,000-25,000)	
Alcohol use	67	21.5
Cigarette use	18	5.8
Use of khat	5	1.6
Use of recreational drugs	6	1.9

4.2.3 Clinical characteristics of HIV positive patients attending clinic at Kenyatta National Hospital

The median time since HIV diagnosis was 11 (7 - 15) years, and the median time since first ART was 9.5 (6 - 14) years. The median Nadir CD4 Count was 26 (20 - 31). Almost all of the patients, 97.1% (303) had viral load less than 1000 copies, 98.1% (306) of the respondents were in WHO stage 1 as shown in Table 4.

Table 4: Clinical characteristics of HIV positive patients attending clinic at Kenyatta National Hospital

Clinical characteristics	**Frequency**	**Percent**
Time since diagnosis (Median (IQR) years	11(7 -15)	
Less or equal 2 years	28	9
3 to 5 years	32	10.3
Above 5 years	252	80.8
Time since first ART (Median (IQR) years	9.5(6 -14)	
Less or equal 2 years	32	10.3
3 to 5 years	34	10.9
Above 5 years	246	78.8
Nadir CD4 count (Median (IQR)	26(20 - 31)	
Current Viral load (within six months)		
Less or equal 50 copies	282	90.4
51 to 500 copies	17	5.4
501 to 1000 copies	4	1.3
More than 1000 copies	9	2.9
Viral load less than 1000 copies/ml		
Yes	303	97.1
No	9	2.9
Current WHO stage		
Stage 1	306	98.1
Stage 2	2	0.6
Stage 3	3	1
Stage 4	1	0.3

4.2.4 Treatment regimen among respondents

85.3% (266) of the study participants were on TDF/3TC/DTG as their current ART regimen. Most of the respondents, 87.5% (273) were on the first line of treatment. 62.2% (194) had history of change of ART regimen. Treatment optimization was the most common reason for ART regimen change occurring among 87.6% (170) of the respondents as shown in Table 5.

Table 5:Treatment regimen among respondents

Clinical characteristics	Frequency	Percent
Current ART		
TDF/3TC/DTG	266	85.3
TDF/3TC/EFV	8	2.6
ABC/3TC/DTG	5	1.6
AZT/3TC/ATV-r	13	4.2
TDF/3TC/ATV-r	19	6.1
AZT/3TC/DTG	1	0.3
Current line ART regimen		
First line	273	87.5
Second line	38	12.2
Third line	1	0.3
History of change of ART regimen		
Yes	194	62.2
No	118	37.8
Type of previous regimen		
AZT/3TC/EFV	9	4.6
TDF/3TC/EFV	128	66
AZT/3TC/NVP	39	20.1
ABC/3TC/LPV-R	3	1.6
TDF/3TC/DTG	6	3.1
TDF/3TC/LPV-R	9	4.6
Duration of use (Median (IQR) years)	6(5)	
Reason for regimen change		
Optimized	170	87.6
Failed	23	11.9
Adverse reaction	1	0.5

4.2.5 Presence of comorbidities among respondents

Further, 25.3% (79) of the respondents had known comorbidities. Of these, 69.6% (55) had hypertension while 16.5% (13) had diabetes. 34.6% (108) had been hospitalized at least once. The average BMI was 26.92 (SD =5.7) while the neck circumference average was 38.04 (SD =3.72) as shown in Table 6.

Table 6: Presence of comorbidities among respondents

Clinical characteristics	Frequency	Percent
Known comorbidity		
Yes	79	25.3
No	233	74.7
Comorbidity present		
Hypertension	55	69.6
Diabetes	13	16.5
Asthma	3	3.8
Others	8	10.1
History of hospitalization		
Yes	108	34.6
No	204	65.4
Number of hospitalizations (Median (IQR)	1(0-2)	
BMI (Mean± SD, kg/m^2)	26.92±5.7	
Underweight	6	1.9
Normal	117	37.5
Overweight	115	36.9
Obesity	74	23.7
Neck circumference (Mean± SD, cm)	38.04±3.72	

4.2.6 Assessment of anxiety and depression among HIV positive patients attending clinic at Kenyatta National Hospital

The findings revealed that anxiety was present in 43.3% (135) of the respondents while depression was present in 31.4% (98) of the respondents as shown in Table 7 (a) and Table 7 (b).

Table 7 (a): Assessment of anxiety among the participants

Anxiety findings	**Frequency**	**Percent**
Anxiety diagnosis		
No anxiety	177	56.7
Mild anxiety	103	33.0
Moderate anxiety	21	6.7
Severe anxiety	11	3.5
Anxiety score		
Present	135	43.3
Absent	177	56.7

Table 7 (b): Assessment of depression among the participants

Depression findings	Frequency	Percent
Depression diagnosis		
No depression	214	68.6
Mild depression	67	21.5
Moderate depression	22	7.1
Moderately severe depression	5	1.6
Severe depression	4	1.3
Depression score		
Present	98	31.4
Absent	214	68.6

4.2.7 The prevalence of poor sleep quality in patients with HIV using the Pittsburgh Sleep Quality Index.

The findings from the study showed that 59.6% (186), (95% CI: 54, 65) of the respondents had poor sleep quality as shown in Table 8.

Table 8: The prevalence of poor sleep quality in patients with HIV.

Sleep quality	**Frequency (%)**	**95%CI (Lower limit, Upper limit)**
Poor sleep quality	186 (59.6)	53, 65

4.2.8 Quality of sleep: component scores of the PSQI in patients with HIV

The quality of sleep components was assessed where the findings revealed that, there was significant difference between poor and good sleep quality across all the components except for sleep efficiency (p =0.759) as shown in Table 9.

Table 9: Quality of sleep: component scores of the PSQI in patients with HIV

	Sleep quality			
Components	**Poor sleep quality**	**Good sleep quality**	**Total n (%)**	**P-value**
Component 1: Subjective sleep quality				
0	71	104	175(56.1)	
1	90	22	112(35.9)	p<0.001
2	19	0	19(6.1)	
3	6	0	6(1.9)	
Component 2: Sleep latency				
0	29	86	115(36.9)	
1	77	34	111(35.6)	
2	45	5	50(16)	p<0.001
3	35	1	36(11.5)	
Component 3: Hours of sleep				
0	65	84	149(47.8)	
1	90	39	129(41.3)	p<0.001
2	24	3	27(8.7)	
3	7	0	7(2.2)	
Component 4: Sleep efficiency				
0	5	4	9(2.9)	
1	5	2	7(2.2)	0.759
2	19	11	30(9.6)	
3	157	109	266(85.3)	
Component 5: Sleep disturbance				
0	10	41	51(16.3)	
1	148	84	232(74.4)	p<0.001
2	26	1	27(8.7)	
3	2	0	2(0.6)	
Component 6: Use of sleep medication				
0	164	126	290(92.9)	
1	13	0	13(4.2)	
2	3	0	3(1.0)	p<0.001
3	6	0	6(1.9)	
Component 7: Daytime dysfunction				
0	93	120	213(68.3)	
1	66	6	72(23.)	
2	23	0	23(7.4)	p<0.001
3	4	0	4(1.3)	

4.2.9 The burden of high risk for obstructive sleep apnea in patients with HIV using the STOP-BANG questionnaire

Obstructive sleep apnea was also investigated in this study. The findings revealed that, 58.7% (183) of the respondents had high risk for obstructive sleep apnea, as shown in Table 10.

Table 10: The burden of high-risk obstructive sleep apnea in patients with HIV.

OSA Risk	Frequency (%)	95%CI
High Risk	183(58.7)	53,64

4.3 Bivariate analysis of the findings

4.3.1 The association between depression, anxiety, and quality of sleep in patients with HIV attending the HIV clinic at KNH.

The results revealed that anxiety and depression were significantly associated with sleep quality. HIV positive patients who had anxiety were 2.7 times more likely to have poor sleep quality, (OR =2.679, 95%CI (1.659, 4.327), p<0.001). Similarly, respondents who had depression were 2.6 times more likely to have poor sleep quality, (OR =2.610, 95%CI (1.54, 4.423), p<0.001) as shown in Table 11.

Table 11: The association between depression, anxiety, and quality of sleep in patients with HIV

	Sleep quality			
	Poor sleep quality (frequency, %)	**Good sleep quality (frequency, %)**	**OR (95%CI)**	**P-value**
Anxiety				
Present	98(52.7)	37(29.4)	2.679(1.659,4.327)	p<0.001
Absent	88(47.3)	89(70.6)	Ref	
Depression				
Present	73(39.2)	25(19.8)	2.610(1.54,4.423)	p<0.001
Absent	113(60.8)	101(80.2)	Ref	

4.3.2 Association between patient demographic characteristics and poor sleep quality

The findings revealed that alcohol use was significantly associated with poor sleep quality (p=0.009) as shown in Table 12.

Table 12: Association between patient demographic characteristics and poor sleep quality

	Sleep quality		
	Poor sleep quality	**Good sleep quality**	**P-value**
Gender			
Male	81(43.5)	52(41.3)	0.389
Female	105(56.5)	74(58.7)	
Age (Mean)	45.45	44.0	0.34
Level of education			
None at all	5(2.7)	5(4)	
Primary	42(22.6)	30(23.8)	0.912
Secondary	75(40.3)	48(38.1)	
Tertiary	64(34.4)	43(34.1)	
Marital status			
Single	60(32.3)	36(28.6)	
Married	91(48.9)	62(49.2)	
Divorced	4(2.2)	4(3.2)	0.871
Widowed	18(9.7)	12(9.5)	
Separated	13(7)	12(9.5)	
Residence			
Urban	154(82.8)	101(80.2)	0.328
Rural	32(17.2)	25(19.8)	
Employment status			
Formally employed	123(66.1)	82(65.1)	0.471
Not employed	63(33.9)	44(34.9)	
Average income (Mean)	20021.0	20246.3	
Alcohol use	45(24.2)	22(17.5)	**0.009**
Cigarette smoking	11(5.9)	7(5.6)	0.551
Use of khat	4(2.2)	1(0.8)	0.329
Use of recreational drugs	3(1.6)	3(2.4)	0.464

4.3.3 Association between disease characteristics and poor sleep quality

The findings revealed that, Current regimen (P = 0.005), history of ART regimen change (p=0.002) and presence of known comorbidity (p =0.044) were significantly associated with poor sleep quality as shown in Table 13.

Table 13: The relationship between disease characteristics and poor sleep quality

	Sleep quality		P-value
	Poor sleep quality	**Good sleep quality**	
Time since diagnosis			
Less or equal 2 years	16(8.6)	12(9.5)	
3 to 5 years	24(12.9)	8(6.3)	0.224
Above 5 years	146(78.5)	106(84.1)	
Time since first ART	10	9.15	
Less or equal 2 years	19(10.2)	13(10.3)	
3 to 5 years	24(12.9)	10(7.9)	0.412
Above 5 years	143(76.9)	103(81.7)	
Nadir CD4 count (Mean)	46	42	0.581
Viral load less than 1000 copies/ml			
Yes	179(96.8)	120(95.2)	0.346
No	6(3.2)	6(4.8)	
Current ART			
TDF/3TC/DTG	152(81.7)	114(90.5)	
TDF/3TC/EFV	3(1.6)	5(4)	
ABC/3TC/DTG	4(2.2)	1(0.8)	**0.005**
AZT/3TC/ATV-r	10(5.4)	3(2.4)	
TDF/3TC/ATV-r	16(8.6)	3(2.4)	
AZT/3TC/DTG	1(0.5)	0	
Current line ART regimen			
First line	159(85.5)	114(90.5)	
Second line	27(14.5)	11(8.7)	0.153
Third line	0	1(0.8)	
History of change of ART regimen			
Yes	117(62.9)	77(61.1)	**0.002**
No	69(37.1)	49(38.9)	
Known comorbidity			
Yes	54(29)	25(19.8)	**0.044**
No	132(71)	101(80.2)	

History of hospitalization			
Yes	68(36.6)	40(31.7)	0.225
No	118(63.4)	86(68.3)	
BMI			
Body mass index			
Underweight	4(2.2)	2(1.6)	
Normal	64(34.4)	53(42.1)	0.588
Overweight	72(38.7)	43(34.1)	
Obesity	46(24.7)	28(22.2)	
Neck Circumference (Mean)	38.18	37.85	0.305

4.3.4 Association between patient demographic characteristics and OSA

The findings showed that gender ($p<0.001$), age ($p<0.001$), marital status ($p<0.001$), employment status, ($p = 0.04$) and cigarette smoking ($p = 0.005$) were significantly associated with high risk of obstructive sleep apnea as shown in Table 14.

Table 14: Association between patient demographic characteristics and OSA

	OSA Risk		
	High Risk	**Low Risk**	**P-value**
Gender			
Male	111(60.7)	22(17.1)	p<0.001
Female	72(39.3)	107(82.9)	
Age (Mean± SD)	47.97±5.12	40.67±8.81	p<0.001
Level of education			
None at all	4(2.2)	6(4.7)	
Primary	40(21.9)	32(24.8)	0.059
Secondary	83(45.4)	40(31)	
Tertiary	56(30.6)	51(39.5)	
Marital status			
Single	39(21.3)	57(44.2)	
Married	109(59.6)	44(34.1)	
Divorced	5(2.7)	3(2.3)	p<0.001
Widowed	17(9.3)	13(10.1)	
Separated	13(7.1)	12(9.3)	
Residence			
Urban	150(82)	105(81.4)	0.506
Rural	33(18)	24(18.6)	
Employment status			
Formally employed	128(69.9)	77(59.7)	
Not employed	55(30.1)	52(40.3)	0.040
Monthly income (Mean± SD	22360.66±15,891	16922.48±10,781	
Alcohol use	42(23)	25(19.4)	0.270
Cigarette smoking	16(8.7)	2(1.6)	0.005
Use of khat	4(2.2)	1(0.8)	0.312
Recreational drug use	4(2.2)	2(1.6)	0.516

4.3.5 Association between disease characteristics and OSA

Presence of known comorbidity (p<0.001), use of additional medication (p<0.001), body mass index (p=0.002) and neck circumference (p =0.001) were significantly associated with high risk of obstructive sleep apnea as illustrated in Table 15.

Table 15: Association between disease characteristics and OSA

	OSA Risk		
	High Risk	**Low Risk**	**P value**
Duration since diagnosis			
Less or equal 2 years	14(7.7)	14(10.9)	
3 to 5 years	23(12.6)	9(7)	0.199
Above 5 years	146(79.8)	106(82.2)	
Duration of ART			
Less or equal 2 years	17(9.3)	15(11.6)	
3 to 5 years	24(13.1)	10(7.8)	0.288
Above 5 years	142(77.6)	104(80.6)	
Nadir CD4 (Mean±SD)	36.3±4.8	50.57±11.193	0.196
Current viral load			
Less or equal 50 copies	164(89.6)	118(91.5)	
51 to 500 copies	12(6.6)	5(3.9)	0.529
501 to 1000 copies	3(1.6)	1(0.8)	
More than 1000 copies	4(2.2)	5(3.9)	
Viral load less than 1000 copies/ml			
Yes	177(97.3)	122(94.6)	0.181
No	5(2.7)	7(5.4)	
Current WHO stage			
Stage 1	181(98.9)	125(96.9)	
Stage 2	1(0.5)	1(0.8)	0.168
Stage 3	0	3(2.3)	
Stage 4	1(0.5)	0	
Current ART			
TDF/3TC/DTG	156(85.2)	110(85.3)	
TDF/3TC/EFV	5(2.7)	3(2.3)	
ABC/3TC/DTG	4(2.2)	1(0.8)	0.741
AZT/3TC/ATV-r	8(4.4)	5(3.9)	
TDF/3TC/ATV-r	9(4.9)	10(7.8)	
AZT/3TC/DTG	1(0.5)	0	
Current line ART regimen			
First line	164(89.6)	109(84.5)	
Second line	19(10.4)	19(14.7)	0.244
Third line	0	1(0.8)	
History of change of ART regimen			
Yes	113(61.7)	81(62.8)	0.473
No	70(38.3)	48(37.2)	
Known comorbidity			
Yes	63(34.3)	16(12.4)	p<0.001
No	120(65.6)	113(87.6)	
Additional medications			
Yes	55(30.2)	12(9.3)	p<0.001

No	127(69.8)	117(90.7)	
History of hospitalization			
Yes	68(37.2)	40(31)	0.158
No	115(62.8)	89(69)	
Body Mass Index			
Underweight	2(1.1)	4(3.1)	
Normal	66(36.1)	51(39.5)	
Overweight	58(31.7)	57(44.2)	0.002
Obesity	57(31.1)	17(13.2)	
Neck Circumference	39.4±3.03	35.85±2.29	0.002

4.4 Multivariable analysis of the findings

4.4.1 Independent factors associated with poor sleep quality

Multivariable analysis was conducted to determine independent predictors of poor sleep quality. The findings showed that, presence of comorbidity, anxiety and depression were independently associated with poor sleep quality. Patients who had a comorbidity were 1.6 times more likely to have poor sleep quality, (aOR:1.554, 95%CI:0.312, 2.983, p =0.044). Patients who had anxiety were 2.2 times more likely to have poor sleep quality, (aOR:2.228, 95%CI:1.29, 3.848, p =0.004). Respondents who had depression were 3.5 times more likely to have poor sleep quality, (aOR:3.535, 95%CI:0.294, 5.972, p =0.040) as shown in Table 16.

Table 16: Independent factors associated with poor sleep quality

Associated factors	aOR(95%CI)	P-value
Alcohol use		
Yes	0.678(0.367,1.254)	0.216
No	Ref	
Current ART		
TDF/3TC/DTG	Ref	
TDF/3TC/EFV	1.34(0.95, 3.561)	0.141
ABC/3TC/DTG	0.123(0.134, 1.314)	0.341
AZT/3TC/ATV-r	0.671(0.121, 1.415)	0.671
TDF/3TC/ATV-r	0.91(0.431, 1.891)	0.091
AZT/3TC/DTG	0.341(0.013, 0.945)	0.121
History of change of ART regimen		
Yes	0.858(0.515,1.432)	0.559
No	Ref	
Known comorbidity		
Yes	1.554(0.312,2.983)	0.044
No	Ref	
Anxiety		
Present	2.228(1.290, 3.848)	0.004
Absent	Ref	
Depression		
Present	3.535(0.294, 5.972)	0.040
Absent	Ref	

.

4.4.2 Independent factors associated with obstructive sleep apnea

The findings revealed that male gender, increase in age, body mass index and neck circumference were independently associated with high risk of OSA. Male patients were 1.2 times more likely to have high risk for OSA compared to women, (aOR:1.158, 95%CI:0.065, 2.561, p <0.001). An increase in one year for a patient was associated with 2.9 times higher chance of high risk for OSA (aOR:2.946, 95%CI:0.912, 4.5111, p =0.003). Those who were overweight were 4.63 times more likely to have high risk of OSA (aOR:4.63, 95%CI:1.752, 12.235, p =0.002). Respondents who were obese were 7.8 times more likely to have high risk of OSA (aOR:7.842, 95%CI:3.087, 19.920, p <0.001). Further, increase in neck circumference was associated with high risk of OSA (aOR:1.677 95%CI:0.587, 4.015, p<0.001) as shown in Table 17.

Table 17: Independent factors associated with obstructive sleep apnea

Factors	aOR(95%CI)	P-value
Gender		
Male	1.158(0.065, 2.561)	P<0.001
Female	Ref	
Age	2.946(0.912,4.511)	0.003
Marital status		0.369
Single	Ref	
Married	0.998(0.248,4.012)	0.997
Divorced	0.880(0.230,3.372)	0.852
Widowed	0.653(0.042,5.154)	0.761
Separated	0.282(0.052,1.4)	0.122
Employment status		
Formally employed	0.674(0.342,1.331)	0.256
Not employed		
Cigarette use		
Yes	0.276(0.047,1.63)	0.155
No	Ref	
Presence of known comorbidity		
Yes	0.38(0.099,1.459)	0.159
No		
Additional medication		
Yes	0.807(0.208,3.128)	0.756
No		
Body Mass index		
Underweight	0.671(0.123,2.191)	0.219
Normal	Ref	
Overweight	4.630(1.752,12.235)	0.002
Obesity	7.842(3.087,19.920)	P<0.001
Neck circumference	1.677(0.587, 4.015)	P<0.001

5 CHAPTER FIVE: DISCUSSION, CONCLUSION AND RECOMMENDATIONS

5.1 DISCUSSION

5.1.1 Quality of sleep of adults with HIV infection

The findings from the present study established that more than half, that is, 59.6% of the respondents had poor sleep quality utilizing the PSQI tool. Our findings are higher than the estimates among populations without HIV, where sleep disturbance has been estimated to range between 13 to 30% (6). There has been a significant relationship between HIV infection and sleep disorders compared to general population. The present findings are consistent with a meta-analysis conducted by Wu et al. that included 27 studies assessing 9,246 HIV positive patients and established that the pooled prevalence of poor sleep quality was 58% (5). The present findings also compare with those from a cross sectional study conducted in an urban tertiary center in Lagos, Nigeria by Oshinaike et al., which found that the prevalence of poor quality of sleep was 59.3% (13). Similarly, Redman et al., in a study conducted at an urban hospital in Soweto South Africa, found that the prevalence of poor sleep quality was 61% among adult patients with HIV (26). The consistency in results could be attributed to the comparable health characteristics of adult patients living with HIV/AIDS in these settings which are within the Sub-Saharan Africa Region. For instance, findings from the present study revealed that the average age of study participants was 44.9 years, which is comparable to the average age of study participants in a study in Cameroon by Balkissou et al. (43.9 years) (40). Similarly, in the study conducted in South Africa by Redman et al., the average age was 42.7 years (26). In a study conducted in Kilifi Kenya among PLHIV, the mean age of study participants was 42.7 years (99). With regard to age, the current study identified that more than half of the respondents, 57.4% were female. The findings are comparable to past studies which have identified that HIV infection in Africa is more prevalent in women. In a study conducted by Ng'ang'a et al. conducted at the KNH HIV clinic, 62.2% of the study population was female(67). In a study conducted in Ethiopia by Degu et al. investigating quality of sleep, 63.7% of the HIV population was female (100). Some studies have shown a different pattern (22,25). Allavena et al. in a study conducted in France found a lower prevalence of poor sleep quality with less than half of the respondents, 47% reporting poor sleep quality (22). A much larger study conducted across China found that 43.1% of PLHIV were poor sleepers (25). The variance between these studies may be attributed to the racial and socioeconomic differences of the various study populations. Several studies have identified that sleep disturbances tend to occur more in people of African descent (101). In addition, studies have linked poor sleep quality to

lower socioeconomic status (102). Furthermore, disparity in health care access and delivery may explain the higher prevalence as sleep disturbances tend to be underrecognized and untreated (103). The present study demonstrates that poor sleep quality is common in adult patients with HIV attending the HIV clinic at Kenyatta National Hospital. Therefore, there is need for clinicians to regularly assess the quality of sleep of adult patients with HIV.

5.1.2 Risk of obstructive sleep apnea in adults with HIV infection

The current study found that 58.7% of the respondents were at high risk for obstructive sleep apnea (OSA) based on the STOP-BANG tool. This finding is significantly higher than estimates in the general population, that vary from 9 to 38% (37). Findings from the present study are comparable to a study conducted in United States by Gutierrez et al. who found that 58% of the HIV population had moderate to high risk of OSA (24). In this cross-sectional study, the STOP-BANG questionnaire was also used. However, the findings from our current study are inconsistent with other studies which have found lower risk of obstructive sleep apnea in adults patients living with HIV (15,40,42). A study conducted in Cameroon by Njoh et al. among PLHIV found that 43.6% had a high risk of obstructive sleep apnea (15). The lower risk of OSA could be attributed to the assessment tool utilized. In our present study, STOP-BANG tool was used while Njoh et al. used the Berlin questionnaire to investigate risk of OSA. The difference in tools used could have an influence on the prevalence of OSA especially considering that both studies were conducted in Sub-Saharan Africa. Yone et al. used the STOP-BANG questionnaire but limited the study population to HAART-naive HIV positive individuals. In this study consisting of 685 participants, 12.7% of the population was at high risk for OSA (42). On the other hand, despite similarity in methodology with our study, a recent study conducted in Nigeria found a much lower prevalence with 20.2% of PLHIV being at high risk of OSA (104). This could be attributed to the difference in BMI. In the present study majority, 60.6% of the respondents were either overweight or obese while in their study 26.8% were obese (104). In comparison to several other studies, HIV patients in our study had relatively higher BMI scores. The mean BMI in our cohort was 26.92±5.7 and majority of participants were either overweight or obese (60.6%). In the study by Odeyemi et al. in Nigeria, the mean BMI was 23.54±4.71 with 26.8% being obese (104). In the study by Balkissou et al. in Cameroon, the median BMI was 24.09 (21.88-27.26) and no association was found between obesity and OSA risk (105). In the study by Yone et al., only 12.7% of PLHIV were at high risk for OSA. 20.3% of participants were either overweight or obese with 64.1% being

underweight. An explanation could be the clinical characteristics of their study population, as all participants were HAART-naïve with about 44% being in CDC stage C (42). The higher average BMI of our study participants may therefore explain the higher prevalence of high risk of OSA in our HIV population. Overweight respondents were 4.63 times more likely to have high risk of OSA while those who were obese were 7.8 times more likely. The high prevalence of high risk for obstructive sleep apnea in the present study may also reflect an overall increase globally. Prevalence of OSA has been increasing significantly over the years including among people living with HIV. A study by Chen et al. in Taiwan revealed that 62.96% of their HIV study population had sleep-related breathing disorders, based on polysomnography findings (106). A USA-based nationwide database analysis found that between 2007 and 2016, there was a 15.5% annual increase in the number of admissions of HIV positive patients with OSA as a comorbidity (107). Our results demonstrate that a high proportion of adults with HIV attending the HIV clinic at Kenyatta National Hospital are at high risk for obstructive sleep apnea. This finding underscores the need for screening of PLHIV for obstructive sleep apnea.

5.1.3 Association between quality of sleep and depression in adults with HIV infection

The present study established that depression was significantly and independently associated with poor quality of sleep among adults with HIV infection. The findings further revealed that adults with HIV infection and depression were 3.5 times more likely to have poor sleep quality. Mengistu et al. in Ethiopia found similar findings where it was established that adult HIV infected patients who were depressed were 3.52 times more likely to have poor sleep quality (108). The association between sleep quality and depression may be attributed to pathophysiological mechanisms such as hypothalamic-pituitary-adrenal axis dysfunction that occur in psychiatric conditions. This is evidenced by findings of polysomnographic studies which have demonstrated alterations in the sleep stages of patients with depression such as reduced REM latency and shortened slow-wave sleep (65). Based on the PHQ-9 tool, 31.4% of respondents in the current study had depression, and this is higher than global and regional estimates (109). Depression is a commonly occurring psychiatric condition among PLHIV which explains the high level in the present study. These findings are in line with a survey conducted in Sub-Saharan Africa among PLHIV, which found the prevalence of depression ranging between 6-59% (110). Another view that has emerged from longitudinal data is that sleep disturbances significantly increase the risk of subsequently developing psychiatric conditions particularly anxiety and depression, thus suggesting

bidirectional causality (65). Therefore, based on our findings, diagnosing depression in PLHIV should prompt assessment of sleep quality. Equally, identifying poor sleep quality should prompt screening for depression in PLHIV.

5.1.4 Association between quality of sleep and anxiety in adults with HIV infection

Findings from the present study established that anxiety was significantly and independently associated with poor quality of sleep. HIV adult patients with anxiety were 2.2 times more likely to have poor sleep quality. Similarly, Daubert et al. in USA found that poor sleep was significantly associated with anxiety symptoms among women with HIV (111). The association between sleep quality and anxiety may also be attributed to pathophysiological mechanisms, evidenced by polysomnographic data revealing increased sleep onset latency, and sleep fragmentation in patients with anxiety (65). Equally, poor sleep quality may in turn induce anxiety symptoms (65). In the present study, 43.3% of respondents had anxiety, which is comparable to a study conducted in Ethiopia by Bedaso et al. where 31.9% of HIV adult patients had anxiety. The variance could be attributed to difference in assessment tools used. In the present study, GAD-7 tool was used to assess anxiety while in their study, the Hospital Anxiety and Depression Scale (HADS) was utilized (112). Nonetheless, anxiety has been shown to occur more commonly in PLHIV than in the general population, and this explains the higher rate observed in our study (109).

Anxiety and depression in PLHIV have been attributed to various factors such as the neuropsychiatric adverse effects of antiretroviral therapy, possible HIV-mediated neuronal injury, and the strain of HIV-associated stigma and chronic disease burden (66). Our findings show that depression and anxiety occur commonly among people living with HIV and are significant associated factors of poor sleep quality in these patients. The results are similar to a large cross-sectional study conducted among PLHIV in China, in which the strongest associations found were between anxiety and depression and poor sleep quality ($p<0.001$) (25). Our findings emphasize the necessity of routinely screening PLHIV for sleep disturbances and also for anxiety and depression. Given the bidirectional cause-effect relationship between anxiety, depression and sleep disturbance, studies indicate that targeted treatment of one may improve the other (65). Identifying and treating anxiety and depression would help in management of poor sleep. Alternatively, managing sleep disturbances may be essential in controlling both depression and anxiety. On the other hand, results of the present study also demonstrated that a significant proportion of HIV infected adults with poor sleep quality did not have depression (that is, 60.8% of poor sleepers) or

anxiety (that is, 47.3% of poor sleepers). This result implies that sleep disturbances in persons living with HIV can occur in the absence of an underlying psychiatric condition. Consequently, it is important to routinely screening PLHIV for sleep disturbances even in the absence of symptoms suggestive of psychiatric disorders.

5.1.5 Factors associated with poor sleep quality and high risk for obstructive sleep apnea

The present study found that, the current regimen of antiretroviral therapy, history of regimen switching, having a comorbidity, and using alcohol were significantly associated with poor quality of sleep. In regard to antiretroviral therapy, majority (85.3%) of participants in our study were on a combination of tenofovir, lamivudine and dolutegravir (TDF/3TC/DTG) as their current ART regimen. The association may be explained by the neuropsychiatric adverse effects associated with the use of dolutegravir. Though the pathophysiological mechanism is unclear, several studies have demonstrated neuropsychiatric side effects such as sleep disturbances, vertigo, and depression with use of integrase inhibitors, particularly dolutegravir (35). This reason may also explain why regimen switching was also significantly associated with poor sleep quality in the present study. History of regimen switching was present in 62.2% of the cases, with the most common indication being to optimize treatment by switching from a NNRTI-based regimen to a DTG-based regimen. In a study conducted at the KNH CCC by Abutika et al., 22.8% of participants switched from an efavirenz-based regimen to a dolutegravir-based regimen experienced neuropsychiatric adverse effects, with 7% experiencing insomnia (113). The association between poor sleep quality and regimen switching may also be explained by the possible psychological impact of changing treatment. A qualitative study conducted in Uganda found that patients switched from efavirenz to dolutegravir experienced worry over being changed to a new regimen, and were concerned about the uncertainty of possible side effects (114). A similar finding was noted in a nationwide cross-sectional study in China, where regimen switching was significantly associated with poor sleep quality (25). Based on the present findings, PLHIV should be screened routinely for possible long-term ART-associated neuropsychiatric adverse effects such as sleep disturbances. Further, in view of the plausible psychological impact of regimen switching, patients changing treatment should undergo adequate counselling including when the indication is treatment optimization.

Bivariate analysis also established that use of alcohol was significantly associated with poor sleep quality. Though a central nervous system depressant, alcohol, with chronic use, has been linked to sleep complaints such as delayed sleep onset, frequent awakenings, and reduced total sleep time.

EEG evidence indicates altered slow wave sleep activity (115). Zakir et al. in Ethiopia found that PLHIV with alcohol use disorder were about 3 times more likely to have poor sleep (116). Despite the lack of association on multivariate analysis between alcohol use and sleep in the present study, sleep quality improvement strategies among PLHIV should maintain measures to identify and control substance abuse, particularly concerning alcohol, based on prevailing evidence in the field. In addition, future studies may explore and characterize further the association between alcohol use and sleep quality in PLHIV in Kenya.

Multivariate analysis established that having a comorbidity, anxiety or depression were independently associated with poor sleep quality. In the present study, participants who had a comorbidity were 1.6 times more likely to have poor sleep quality. Various studies have described an association between poor sleep quality and the presence of comorbidities. Gutierrez et al. in the United States found that presence of comorbid illnesses such as hypertension and diabetes was significantly associated with poor sleep in PLHIV (24). The association may be attributable to the specific comorbidity present, where a disease process is implicated in disruption of normal sleep physiology. Further, sleep disturbances may also predispose to the onset or progression of disease. Majority of participants with comorbidities in the present study had either hypertension or diabetes mellitus, both of which have been shown to be significantly associated with poor sleep (76). In addition, the association between sleep quality and comorbidities may be due to psychological factors such as stress of pill burden, financial strain of accessing treatment, and also possible disease-related stigma. A linear relationship has also been suggested between severity of poor sleep and the number of comorbidities present. A cross-sectional study conducted in Japan by Hayashino et al. found that sleep quality declined further with increase in the number of comorbid conditions (117). Our present findings suggest that HIV infected patients with comorbidities are at increased risk for poor sleep quality thus should be screened regularly for sleep disturbances.

Current findings revealed that there was no significant association between HIV viral load, CD4 count, duration of infection, and quality of sleep. There is less definitive understanding on the link between sleep quality and factors specific to HIV disease such as viral load and CD4 cell count. The lack of association in the present study is consistent with findings of Crum-Cianflone et al. in USA, Allavena et al. in France, Huang et al. in China, and Bedaso et al. in Ethiopia (19,22,25,112). In addition, a systematic review by Reid and Dwyer found that sleep disturbances were frequent

in all stages of HIV disease and were not related to severity of illness or categorical stages of HIV infection (7). On the other hand, some studies have linked poor sleep quality in PLHIV with immune status. Oshinaike et al. found that lower CD4 counts were associated with poor sleep quality. Similarly, Desalu et al. in Nigeria, Seay et al. in USA, and Rodriguez et al. in Mexico also found an association with lower CD4 counts (13,14,20,27). This would seem to be the more probable situation, given the reports of HIV-associated neurotoxicity, and also the association between lower immune status, disease progression and overall poor health outcomes. Conversely, Redman et al. in South Africa found that poor sleep quality was associated with higher CD4 change from baseline and higher current CD4 levels. Their finding implies an underlying HIV-associated chronic immune activation mediating sleep disturbances, even in the presence of viral suppression (26). This hypothesis may be supported by a study by Roca C et al. which demonstrated reduced brain mitochondrial DNA content despite HIV viral suppression (53). Considering this perspective, the absence of a significant association between CD4 count and sleep quality in the present study may be attributed to the lack of sufficient data for significant statistical computations. CD4 level testing is no longer conducted routinely at the KNH CCC thus data on current CD4 level was lacking. Future studies should investigate the HIV-specific immunopathological mechanisms contributing to sleep disorders in order to develop treatment interventions that are best tailored towards people living with HIV.

The findings from the present study determined under bivariate analysis that presence of a comorbidity, use of additional medication, cigarette smoking, marital status, employment status, gender, age, body mass index, and neck circumference, were associated with high risk of obstructive sleep apnea. Having a comorbidity increased risk for obstructive sleep apnea. This is comparable to a study by Chen et al. in Taiwan which found that presence of comorbidities was associated with sleep disordered breathing in PLHIV. In their study, an increase in the number of comorbid illnesses present was associated with an increase in severity of sleep disordered breathing (106). About 25% of participants in the present study had comorbidities. These comprised mainly of hypertension (about 70% of the cases), and diabetes mellitus (about 16% of the cases). Obstructive sleep apnea has been linked to hypertension and diabetes(76,78). It is suggested that the sleep disruption and intermittent repetitive hypoxia that occur in OSA alter the hypothalamic-pituitary-adrenal (HPA) axis and induce sympathetic hyperactivity triggering or

worsening hypertension, insulin resistance, and reduction in basal metabolic rate(75,79). Therefore, screening for and treating obstructive sleep apnea may aid in controlling comorbid illnesses such as hypertension or diabetes. Furthermore, evidence that is emerging suggests that metabolic disorders such as diabetes mellitus can also worsen OSA. This proposes a bidirectional relationship between OSA and cardiometabolic diseases (118). In view of this and the findings of the present study, patients with HIV and comorbid illnesses such as hypertension and diabetes mellitus should be screened for sleep disturbances including obstructive sleep apnea. In addition, risk of obstructive sleep apnea can be mitigated by controlling comorbid illnesses in these patients particularly diabetes mellitus, hypertension, and obesity.

The present study identified that use of additional medications (other than antiretroviral therapy) was associated with high risk of obstructive sleep apnea. Pathophysiological models of OSA do not usually integrate the possible role of prescription medications, despite the common use of medication by patients with obstructive sleep apnea. In the current study, this association may be linked to the presence of comorbidities, as patients with conditions such as diabetes and hypertension are frequently on multiple prescription drugs. Smith et al. investigated the association between the use of common prescription medication and sleep patterns of patients with untreated obstructive sleep apnea. They found that antidepressant and anxiolytic drugs affected the sleep architecture of patients with OSA but found no association with other medications such as antidiabetics or antihypertensives (119). The effects of common or frequent medication combinations on risk of OSA may be investigated in future research.

The results of the present study also revealed that under bivariate analysis, cigarette smoking was associated with high risk of obstructive sleep apnea. This is similar to findings of Njoh et al. in Cameroon, however, like in our present study, it was found to be a confounding factor (15). Nevertheless, in another study conducted in Cameroon, Yone et al. found that smoking was an independent determinant of high risk of OSA (42). It is postulated that cigarette smoking may cause or aggravate obstructive sleep apnea through modifications in sleep structure and arousal threshold, upper airway neuromuscular control, and by inducing airway inflammation. On the other hand, untreated OSA has been linked to smoking addiction(120). The role and impact of smoking in OSA among HIV patients is not clearly defined owing to small proportions of smokers in similar study populations. A meta-analysis by Taveira et al. on the relationship between OSA

and tobacco use could not confirm an association due to limited available evidence (121). Our finding demonstrates the plausible association between smoking and risk for OSA thus, future studies are required to expound this relationship, given that smoking is a modifiable and avertable risk factor.

In the present study, marital status was associated with high risk for obstructive sleep apnea whereby cases at high risk for OSA were more likely to be married than single. In a study by Charokopos et al., subjects who were married were over two times more likely to have moderate to severe OSA (122). The reasons for this association are unclear, however, there are some postulates. It could be hypothesized that people with bed partners are likely to report sleep related complaints because of observation of symptoms such as snoring by their partners. Further, various studies have found higher rates of overweight/obesity in married adults, compared to those single or divorced/separated. Higher rates of obesity in married persons may explain the higher risk for obstructive sleep apnea observed(123). Employment status was also associated with risk for obstructive sleep apnea on bivariate analysis. Compared to those with low risk, cases at high risk for OSA were more likely to be employed than unemployed. This is unlike findings in more developed countries where high risk of OSA is associated with lower socioeconomic status, which has been ascribed to various factors such as the limitations to quality healthcare and sedentary lifestyle of lower socioeconomic groups (124). The difference observed in our study may be attributed to a plausible association between being employed and being overweight/obese, which is an established risk factor for OSA. Whereas overweight/obesity is more common in the lower socioeconomic strata of developed countries, in developing countries, obesity tends to be more prevalent in higher socioeconomic strata(125). However, given the lack of independent association in our study, the role of socioeconomic status on risk of obstructive sleep apnea in PLHIV in Kenya would require further investigation.

Multivariate analysis in the present study found that, male gender, increasing age, BMI, and neck circumference were independently associated with high risk of OSA. These factors have also been identified in several other studies conducted among PLHIV. Odeyemi et al. used the STOP-BANG questionnaire in a cross-sectional study in Nigeria. With a study population of 198 PLHIV, age, gender, BMI, and neck circumference were found to be significantly associated with risk of OSA (104). Obesity is a recognized and vital risk factor of obstructive sleep apnea. In a study conducted

in the United States, Lo Re et al. found that increased neck circumference, overweight or obese body mass index, and lipodystrophy were potential risk factors for OSA among HIV patients (48). Samaneh et al. investigated the association between BMI and risk of OSA in patients with HIV in Iran and found that each unit increase in BMI increased the odds of being at high risk for OSA by 6% (126). Excess weight gain may result in fat deposition in the neck, and this may subsequently result in mechanical restriction of the airway. Furthermore, accumulation of fat in the abdomen and thorax may in turn reduce compliance of the chest resulting in increase in respiratory effort (127). The significant association between neck circumference and high risk for obstructive sleep apnea in our study is therefore not uncommon, given that neck circumference is not only a marker of obesity, but also a recognized risk factor for obstructive sleep apnea independent of waist circumference (128). With regard to gender and risk for obstructive sleep apnea, studies in BMI-matched men and women demonstrate that men tend to have more severe sleep-disordered breathing. Men have a larger upper body fat distribution than lower body distribution. Moreover, men tend to have larger neck circumferences than women, with a larger soft palate and tongue and a longer oropharynx, which worsen collapsibility. Further, it is hypothesized that various hormones affect the neural and central mechanisms of respiratory control. It is postulated that either the lower testosterone levels or the higher estrogen and progesterone levels in women may be defensive against the development of OSA. Aging is another factor known to be independently associated with obstructive sleep apnea in the general population. Studies have shown that airway muscle responses diminish with increasing age while pharyngeal fat pads increase in size (129). Nevertheless, some studies conducted among PLHIV have found some contrasting findings. In a study conducted in a HIV-positive HAART-naïve population in Cameroon, age, male sex, and smoking history were independent determinants of OSA but BMI was not(42). This could be attributed to the difference in the populations under study whereby the present study included HIV-infected patients on HAART. This is consistent with Brown et al. who evaluated the utility of anthropometry in screening for sleep disordered breathing (SDB) among HIV positive patients. They found that BMI, waist circumference & neck circumference had better predictive value for sleep-disordered breathing in HIV uninfected patients and in HIV infected patients on HAART. In contrast, these parameters were not at all predictive among HIV infected HAART naïve patients (49). Findings from the present study suggest that HIV infected patients on antiretroviral therapy are subject to the effect of traditional risk factors for obstructive sleep apnea such as increasing

age and BMI, and the higher risk associated with male gender. Clinicians caring for HIV infected patients with these characteristics should inquire about suggestive symptoms such as snoring and consider evaluation for sleep disorders particularly obstructive sleep apnea. In addition, addressing modifiable risk factors such as obesity can reduce the risk for obstructive sleep apnea. Therefore, beyond weight assessment, clinicians should institute programs to manage overweight / obesity in routine HIV clinical care.

The present study found no significant association between antiretroviral therapy and risk for OSA. This finding has been corroborated by earlier studies (15,24,43,104). Some antiretroviral drugs in current use such as protease inhibitors (PIs) have been associated with lipodystrophy and dyslipidemia (46). However, data on their contribution to risk or severity of obstructive sleep apnea is limited. Abdeen et al. conducted a retrospective cohort study in the United States and found no significant association between duration of use of protease inhibitors and severity of OSA in PLHIV(130). The lack of significant association between risk for OSA and antiretroviral therapy in the present study may be because of a smaller proportion of patients being on PIs thus limiting statistical comparison. Majority of our study participants were on a dolutegravir-based regimen (85.3%) with only 10.3% being on a PI-based regimen. This is therefore prospect for future research. On the other hand, the newer agents, that is, integrase inhibitors (particularly dolutegravir), have also been associated with weight gain and obesity (113,131). There is however limited data on the magnitude of dolutegravir associated-weight gain on risk of obstructive sleep apnea. Given that majority of our patients were on a dolutegravir-based regimen, the lack of association may also be because weight gain in PLHIV is dependent on multiple factors. Besides the link with antiretroviral therapy, the rise in obesity among PLHIV may also be secondary to shifting demographics, a predisposing social environment (physical inactivity and a high-fat diet), and the effect of aging whereby hormonal changes predispose to the accumulation of body fat (132). With better treatment outcomes, PLHIV are living longer hence are now subject to cardiovascular and metabolic disease risk factors common to the general population. There is therefore need for the establishment of specific measures and programs to address modifiable risk factors such as obesity in order to mitigate risk of obstructive sleep apnea in people living with HIV.

5.2 CONCLUSION

The present study found that among adult patients with HIV infection attending the HIV outpatient clinic at the Kenyatta National Hospital, poor sleep quality was prevalent at 59.6%, while high risk for obstructive sleep apnea was prevalent at 58.7%. Having anxiety, depression, or comorbidity was significantly associated with poor sleep quality. Male gender, increase in age, high body mass index and neck circumference were independently associated with high risk for obstructive sleep apnea. These findings therefore highlight the need to develop policies for screening PLHIV for sleep disorders, and guidelines for addressing modifiable risk factors in order to improve clinical outcomes and overall quality of life.

5.3 STUDY STRENGTHS

This is among the first studies done in Kenya that investigated the quality of sleep and risk of obstructive sleep apnea among people living with HIV. It can be used as a baseline to generate hypothesis for future studies. We screened for both quality of sleep and risk of obstructive sleep apnea. In addition, we screened for comorbid conditions specifically anxiety, depression, and obesity, which helps in the development of possible treatment strategies for sleep disturbances among persons living with HIV in our population.

5.4 STUDY LIMITATIONS

There may have been recall bias while filling out the questionnaires since the participants were being asked to remember information for about one month back. Nonetheless, this limitation was minimized by the use of validated study questionnaires which consider recall bias. Some of the analysis findings might not be representative of the real situation in the target population owing to a small sample size in some cells (n=<5).

5.5 RECOMMENDATIONS

On the basis of the present findings, it is recommended that clinicians prioritize the screening of PLHIV for sleep disturbances including obstructive sleep apnea, regardless of disease stage. Addressing modifiable risk factors such as obesity, anxiety, and depression may significantly improve the sleep quality and overall quality of life of PLHIV. In addition, given the bidirectional relationship between sleep disorders and psychiatric disorders, recognition of sleep disturbances should prompt further evaluation of the patient for a psychiatric disorder such as anxiety or

depression. Future studies may build on this preliminary study to explore quality of sleep and risk of obstructive sleep apnea in people living with HIV in heterogeneous populations through a large cohort study.

REFERENCES

1. Global HIV & AIDS statistics — 2020 fact sheet | UNAIDS [Internet]. 2019 [cited 2020 Dec 2]. Available from: https://www.unaids.org/en/resources/fact-sheet
2. Kenya UNAIDS AIDS Statistics. Kenya | UNAIDS [Internet]. Country factsheets. 2018 [cited 2020 Dec 2]. Available from: https://www.unaids.org/en/regionscountries/countries/kenya
3. De Coninck Z, Hussain-Alkhateeb L, Bratt G, Ekström AM, Gisslén M, Petzold M, et al. Non-AIDS mortality is higher among successfully treated people living with HIV compared with matched HIV-negative control persons: A 15-year follow-up cohort study in Sweden. AIDS Patient Care STDS. 2018 Aug 1;32(8):297–305.
4. Feinstein MJ, Hsue PY, Benjamin LA, Bloomfield GS, Currier JS, Freiberg MS, et al. Characteristics, Prevention, and Management of Cardiovascular Disease in People Living with HIV: A Scientific Statement from the American Heart Association. Circulation [Internet]. 2019 Jul 9 [cited 2020 Feb 26];140(2):e98–124. Available from: http://www.ncbi.nlm.nih.gov/pubmed/31154814
5. Wu J, Wu H, Lu C, Guo L, Li P. Self-reported sleep disturbances in HIV-infected people: A meta-analysis of prevalence and moderators. Sleep Med [Internet]. 2015 Aug [cited 2020 Apr 5];16(8):901–7. Available from: http://www.ncbi.nlm.nih.gov/pubmed/26188954
6. Knutson K. Sleep and pain: Summary of the 2015 Sleep in America Poll [Internet]. Vol. 1, Sleep Health. Elsevier Inc; 2015 [cited 2020 Apr 10]. p. 85. Available from: http://www.ncbi.nlm.nih.gov/pubmed/29073381
7. Reid S, Dwyer J. Insomnia in HIV infection: A systematic review of prevalence, correlates, and management. Vol. 67, Psychosomatic Medicine. 2005. p. 260–9.
8. Opp MR, Krueger JM. Sleep and immunity: A growing field with clinical impact. Vol. 47, Brain, Behavior, and Immunity. Academic Press Inc.; 2015. p. 1–3.
9. Low Y, Goforth HW, Omonuwa T, Preud'homme X, Edinger J, Krystal A. Comparison of polysomnographic data in age-, sex- and Axis I psychiatric diagnosis matched HIV-seropositive and HIV-seronegative Insomnia Patients. Clin Neurophysiol. 2012 Dec 1;123(12):2402–5.
10. Medic G, Wille M, Hemels MEH. Short- and long-term health consequences of sleep disruption [Internet]. Vol. 9, Nature and Science of Sleep. Dove Press; 2017 [cited 2020 May 12]. p. 151–61. Available from: https://www.dovepress.com/short--and-long-term-health-consequences-of-sleep-disruption-peer-reviewed-article-NSS
11. Ramlee F, Sanborn AN, Tang NKY. What Sways People's Judgment of Sleep Quality? A Quantitative Choice-Making Study With Good and Poor Sleepers. Sleep [Internet]. 2017 May 19;40(7). Available from: https://doi.org/10.1093/sleep/zsx091
12. Lee KA, Gay C, Portillo CJ, Coggins T, Davis H, Pullinger CR, et al. Types of sleep problems in adults living with HIV/AIDS. J Clin Sleep Med [Internet]. 2012 Feb 15 [cited 2020 Feb 20];8(1):67–75. Available from: http://jcsm.aasm.org/doi/10.5664/jcsm.1666
13. Oshinaike O, Akinbami A, Ojelabi O, Dada A, Dosunmu A, John Olabode S. Quality of

sleep in an HIV population on antiretroviral therapy at an urban tertiary centre in Lagos, Nigeria. Neurol Res Int. 2014;2014.

14. Desalu O, Aladesanmi A, Ojuawo O, Opeyemi C, Ozoh O, Olarinoye J, et al. Sleep quality, under-recognition and underreporting of sleep disturbance among HIV patients attending tertiary hospital in Ilorin, Nigeria. In: European Respiratory Journal. European Respiratory Society (ERS); 2018. p. PA2545.

15. Njoh AA, Mbong EN, Mbi VO, Mengnjo MK, Nfor LN, Ngarka L, et al. Likelihood of obstructive sleep apnea in people living with HIV in Cameroon – preliminary findings. Sleep Sci Pract [Internet]. 2017 Dec 6 [cited 2020 Feb 25];1(1):4. Available from: http://sleep.biomedcentral.com/articles/10.1186/s41606-016-0003-2

16. Alex LR, Uchôa re, Oliveira MDCDS, Silva AUDA Da, Veras VS, Sousa DF De, et al. Poor Sleep Quality in Persons Living with HIV: A Systematic Review and Meta-Analysis. Res Rev J Nurs Heal Sci. 2018 May 30;4(2):26–33.

17. Cruess DG, Antoni MH, Gonzalez J, Fletcher MA, Klimas N, Duran R, et al. Sleep disturbance mediates the association between psychological distress and immune status among HIV-positive men and women on combination antiretroviral therapy. J Psychosom Res. 2003 Mar 1;54(3):185–9.

18. Salahuddin N, Barroso J, Leserman J, Harmon JL, Pence BW. Daytime Sleepiness, Nighttime Sleep Quality, Stressful Life Events, and HIV-Related Fatigue. J Assoc Nurses AIDS Care [Internet]. 2009 Jan [cited 2020 Apr 6];20(1):6–13. Available from: http://www.ncbi.nlm.nih.gov/pubmed/19118766

19. Crum-Cianflone NF, Roediger MP, Moore DJ, Hale B, Weintrob A, Ganesan A, et al. Prevalence and factors associated with sleep disturbances among early-treated HIV-infected persons. Clin Infect Dis [Internet]. 2012 May [cited 2020 Feb 20];54(10):1485–94. Available from: http://www.ncbi.nlm.nih.gov/pubmed/22431801

20. Seay JS, McIntosh R, Fekete EM, Fletcher MA, Kumar M, Schneiderman N, et al. Self-reported sleep disturbance is associated with lower CD4 count and 24-h urinary dopamine levels in ethnic minority women living with HIV. Psychoneuroendocrinology. 2013 Nov;38(11):2647–53.

21. Gamaldo CE, Spira AP, Hock RS, Salas RE, McArthur JC, David PM, et al. Sleep, function and HIV: A multi-method assessment. AIDS Behav. 2013;17(8):2808–15.

22. Allavena C, Guimard T, Billaud E, de la Tullaye S, Reliquet V, Pineau S, et al. Prevalence and risk factors of sleep disturbances in a large HIV-infected adult population. J Int AIDS Soc. 2014 Nov;17:19576.

23. Faraut B, Malmartel A, Ghosn J, Duracinsky M, Leger D, Grabar S, et al. Sleep Disturbance and Total Sleep Time in Persons Living with HIV: A Cross-Sectional Study. AIDS Behav. 2018 Sep 1;22(9):2877–87.

24. Gutierrez J, Tedaldi EM, Armon C, Patel V, Hart R, Buchacz K. Sleep disturbances in HIV-infected patients associated with depression and high risk of obstructive sleep apnea. SAGE Open Med. 2019 Jan;7:205031211984226.

25. Huang X, Li H, Meyers K, Xia W, Meng Z, Li C, et al. Burden of sleep disturbances and associated risk factors: A cross-sectional survey among HIV-infected persons on

antiretroviral therapy across China. Sci Rep [Internet]. 2017 Dec 1 [cited 2020 Feb 25];7(1):3657. Available from: http://www.ncbi.nlm.nih.gov/pubmed/28623361

26. Redman KN, Karstaedt AS, Scheuermaier K. Increased CD4 counts, pain and depression are correlates of lower sleep quality in treated HIV positive patients with low baseline CD4 counts. Brain Behav Immun. 2018 Mar 1;69:548–55.

27. Rodríguez-Estrada E, Iglesias-Chiesa MC, Fresán-Orellana A, Reyes-Terán G. Factors associated with poor sleep quality among HIV-positive individuals in Mexico City. Salud Ment [Internet]. 2018 [cited 2020 Apr 5];41(3):123–9. Available from: www.revistasaludmental.mx

28. Ohayon MM. Epidemiology of insomnia: What we know and what we still need to learn. Vol. 6, Sleep Medicine Reviews. W.B. Saunders Ltd; 2002. p. 97–111.

29. Roth T. Insomnia: Definition, prevalence, etiology, and consequences. Vol. 3, Journal of Clinical Sleep Medicine. American Academy of Sleep Medicine; 2007. p. S7.

30. Rubinstein ML, Selwyn PA. High prevalence of insomnia in an outpatient population with HIV infection. J Acquir Immune Defic Syndr Hum Retrovirology [Internet]. 1998 Nov 1 [cited 2020 Feb 20];19(3):260–5. Available from: http://www.ncbi.nlm.nih.gov/pubmed/9803968

31. Low Y, Goforth H, Preud'Homme X, Edinger J, Krystal A. Insomnia in HIV-infected patients: Pathophysiologic implications. AIDS Rev. 2014;16(1):3–13.

32. Adeoti AO. Burden of Insomnia and Associated Risk Factors in People Living with HIV/AIDS in a Tertiary Hospital in Sub-Saharan Africa. AIDS Clin Res STDs [Internet]. 2018 [cited 2020 Apr 17];5(1):1–4. Available from: https://www.researchgate.net/publication/328406592

33. Treisman GJ, Soudry O. Neuropsychiatric Effects of HIV Antiviral Medications. Vol. 39, Drug Safety. Springer International Publishing; 2016. p. 945–57.

34. Apostolova N, Funes HA, Blas-Garcia A, Galindo MJ, Alvarez A, Esplugues J V. Efavirenz and the CNS: what we already know and questions that need to be answered. J Antimicrob Chemother [Internet]. 2015 Jul 22;70(10):2693–708. Available from: https://doi.org/10.1093/jac/dkv183

35. Hill AM, Mitchell N, Hughes S, Pozniak AL. Risks of cardiovascular or central nervous system adverse events and immune reconstitution inflammatory syndrome, for dolutegravir versus other antiretrovirals: Meta-analysis of randomized trials [Internet]. Vol. 13, Current Opinion in HIV and AIDS. Lippincott Williams and Wilkins; 2018 [cited 2020 Dec 5]. p. 102–11. Available from: https://pubmed.ncbi.nlm.nih.gov/29278532/

36. Young T, Palta M, Dempsey J, Skatrud J, Weber S, Badr S. The Occurrence of Sleep-Disordered Breathing among Middle-Aged Adults. N Engl J Med. 1993 Apr 29;328(17):1230–5.

37. Senaratna C V., Perret JL, Lodge CJ, Lowe AJ, Campbell BE, Matheson MC, et al. Prevalence of obstructive sleep apnea in the general population: A systematic review. Vol. 34, Sleep Medicine Reviews. W.B. Saunders Ltd; 2017. p. 70–81.

38. Adewole OO, Hakeem A, Fola A, Anteyi E, Ajuwon Z, Erhabor G. Obstructive sleep

apnea among adults in Nigeria. J Natl Med Assoc. 2009;101(7):720–5.

39. Rutagarama O, Gelaye B. Risk of Common Mental Disorders in Relation to Symptoms of Obstructive Sleep Apnea Syndrome among Ethiopian College Students. J Sleep Disord Treat Care. 2015;04(03).

40. A.D. B, E. P-Y, C. K-K, M. M. Prevalence and determinants of obstructive sleep apnea in semi-urban and rural area of cameroon. Am J Respir Crit Care Med [Internet]. 2017 [cited 2020 May 19];195. Available from: www.atsjournals.org

41. Epstein LJ, Strollo PJ, Donegan RB, Delmar J, Hendrix C, Westbrook PR. Obstructive sleep apnea in patients with human immunodeficiency virus (HIV) disease. Sleep [Internet]. 1995 [cited 2020 May 19];18(5):368–76. Available from: https://www.ncbi.nlm.nih.gov/pubmed/7676171

42. E.W. PY, A. B, E. N-K, C. K. Prevalence and determinants of high risk of obstructive sleep apnea in HIV-infected subjects naive to antiretroviral therapy. Am J Respir Crit Care Med [Internet]. 2017 [cited 2020 May 21];195. Available from: www.atsjournals.org

43. Patil SP, Brown TT, Jacobson LP, Margolick JB, Laffan A, Johnson-Hill L, et al. Sleep disordered breathing, fatigue, and sleepiness in HIV-infected and -uninfected men. PLoS One. 2014 Jul 3;9(7).

44. Chen YC, Lin CY, Li CY, Zhang Y, Ko WC, Ko NY. Obstructive sleep apnea among HIV-infected men in the highly active antiretroviral therapy era: a nation-wide longitudinal cohort study in Taiwan, 2000–2011. Sleep Med. 2020 Jan 1;65:89–95.

45. Kunisaki KM, Akgün KM, Fiellin DA, Gibert CL, Kim JW, Rimland D, et al. Prevalence and correlates of obstructive sleep apnoea among patients with and without HIV infection. HIV Med [Internet]. 2015 Feb 1 [cited 2020 Apr 17];16(2):105–13. Available from: http://www.ncbi.nlm.nih.gov/pubmed/25230851

46. Flint OP, Noor MA, Hruz PW, Hylemon PB, Yarasheski K, Kotler DP, et al. The role of protease inhibitors in the pathogenesis of HIV-associated lipodystrophy: Cellular mechanisms and clinical implications. Vol. 37, Toxicologic Pathology. NIH Public Access; 2009. p. 65–77.

47. Patil SP, Schneider H, Schwartz AR, Smith PL. Adult obstructive sleep apnea: Pathophysiology and diagnosis. Chest. 2007;132(1):325–37.

48. Lo Re V, Schutte-Rodin S, Kostman JR. Obstructive sleep apnoea among HIV patients. Vol. 17, International Journal of STD and AIDS. Int J STD AIDS; 2006. p. 614–20.

49. Brown TT, Patil SP, Jacobson LP, Margolick JB, Laffan AM, Godfrey RJ, et al. Anthropometry in the prediction of sleep disordered breathing in HIV-positive and HIV-negative men. Antivir Ther. 2010;15(4):651–9.

50. Taibi DM. Sleep Disturbances in Persons Living With HIV. J Assoc Nurses AIDS Care. 2013 Jan;24(SUPPL. 1):S72-85.

51. Yadav A, Collman RG. CNS inflammation and macrophage/microglial biology associated with HIV-1 infection. Vol. 4, Journal of Neuroimmune Pharmacology. NIH Public Access; 2009. p. 430–47.

52. Bagashev A, Sawaya BE. Roles and functions of HIV-1 Tat protein in the CNS: An

overview. Virol J. 2013 Dec 21;10:358.

53. Roca C, Lim LY PB. Excess Mitochondrial DNA Damage in Brain of People With HIV [Internet]. 7th International Workshop on HIV and Aging, 2017. [cited 2020 Apr 11]. Available from: http://www.natap.org/2016/AGE/AGE_11.htm

54. Eban-Rothschild A, Appelbaum L, De Lecea L. Neuronal Mechanisms for Sleep/Wake Regulation and Modulatory Drive. Vol. 43, Neuropsychopharmacology. Nature Publishing Group; 2018. p. 937–52.

55. Opp MR, Rady PL, Hughes TK, Cadet P, Tyring SK, Smith EM. Human immunodeficiency virus envelope glycoprotein 120 alters sleep and induces cytokine mRNA expression in rats [published errata appear in Am J Physiol 1996 Aug;271(2 Pt 2):section R following table of contents and 1996 Dec;271(6 Pt 3):section R following table of contents]. Am J Physiol Integr Comp Physiol. 1996 May 1;270(5):R963–70.

56. Foster SB, Lu M, Glaze DG, Reuben JM, Harris LL, Cohen EN, et al. Associations of cytokines, sleep patterns, and neurocognitive function in youth with HIV infection. Clin Immunol. 2012 Jul;144(1):13–23.

57. Lee KA, Gay C, Pullinger CR, Hennessy MD, Zak RS, Aouizerat BE. Cytokine Polymorphisms are Associated with Poor Sleep Maintenance in Adults Living with Human Immunodeficiency Virus/Acquired Immunodeficiency Syndrome. Sleep. 2014 Mar 1;37(3):453–63.

58. Kapsimalis F, Basta M, Varouchakis G, Gourgoulianis K, Vgontzas A, Kryger M. Cytokines and pathological sleep. Vol. 9, Sleep Medicine. Elsevier; 2008. p. 603–14.

59. Darko DF, Miller JC, Gallen C, White J, Koziol J, Brown SJ, et al. Sleep electroencephalogram delta-frequency amplitude, night plasma levels of tumor necrosis factor α, and human immunodeficiency virus infection. Proc Natl Acad Sci U S A. 1995 Dec 19;92(26):12080–4.

60. Womack JA, Murphy TE, Bathulapalli H, Akgün KM, Gibert C, Kunisaki KM, et al. Trajectories of Sleep Disturbance Severity in HIV-Infected and Uninfected Veterans. J Assoc Nurses AIDS Care. 2017 May 1;28(3):431–7.

61. Hoffmann C, Llibre JM. Neuropsychiatric adverse events with dolutegravir and other integrase strand transfer inhibitors. AIDS Rev. 2019 Jan 1;21(1):4–10.

62. Parker R, Stein DJ, Jelsma J. Pain in people living with HIV/AIDS: A systematic review. Vol. 17, Journal of the International AIDS Society. 2014.

63. Aguiar GPS de, Dussán-Sarria JA, Souza A de. Sleep alterations in patients with the human immunodeficiency virus and chronic pain. Brazilian J Pain. 2019;2(2):123–31.

64. Nokes KM, Kendrew J. Correlates of sleep quality in persons with HIV disease. J Assoc Nurses AIDS Care [Internet]. 2001 [cited 2020 Apr 23];12(1):17–22. Available from: http://www.ncbi.nlm.nih.gov/pubmed/11211669

65. Krystal AD. Psychiatric Disorders and Sleep. Vol. 30, Neurologic Clinics. NIH Public Access; 2012. p. 1389–413.

66. Chaponda M, Aldhouse N, Kroes M, Wild L, Robinson C, Smith A. Systematic review of the prevalence of psychiatric illness and sleep disturbance as co-morbidities of HIV

infection in the UK [Internet]. Vol. 29, International Journal of STD and AIDS. SAGE Publications Ltd; 2018 [cited 2020 Apr 17]. p. 704–13. Available from: http://www.ncbi.nlm.nih.gov/pubmed/29393007

67. Ng'ang'a P. Prevalence Of Anxiety And Depression Among Hiv/aids Patients Attending The Comprehensive Care Centre (CCC), Kenyatta National Hospital (KNH). J Health Psychol. 2014;13(4):547–55.

68. Unruh ML, Redline S, An MW, Buysse DJ, Nieto FJ, Yeh JL, et al. Subjective and objective sleep quality and aging in the sleep heart health study. J Am Geriatr Soc. 2008 Jul 1;56(7):1218–27.

69. Horvath S, Levine AJ. HIV-1 Infection Accelerates Age According to the Epigenetic Clock. J Infect Dis [Internet]. 2015 Nov 15 [cited 2020 Apr 18];212(10):1563–73. Available from: http://www.ncbi.nlm.nih.gov/pubmed/25969563

70. Islam FM, Wu J, Jansson J, Wilson DP. Relative risk of cardiovascular disease among people living with HIV: A systematic review and meta-analysis. HIV Med. 2012 Sep;13(8):453–68.

71. Sobieszczyk ME, Hoover DR, Anastos K, Mulligan K, Tan T, Shi Q, et al. Prevalence and predictors of metabolic syndrome among HIV-infected and HIV-uninfected women in the women's interagency HIV Study. J Acquir Immune Defic Syndr [Internet]. 2008 Jul 1 [cited 2020 Feb 26];48(3):272–80. Available from: http://www.ncbi.nlm.nih.gov/pubmed/18545157

72. Neuhaus J, Jacobs, Jr DR, Baker JV, Calmy A, Duprez D, La Rosa A, et al. Markers of Inflammation, Coagulation, and Renal Function Are Elevated in Adults with HIV Infection. J Infect Dis [Internet]. 2010 Jun 15 [cited 2020 Apr 21];201(12):1788–95. Available from: http://www.ncbi.nlm.nih.gov/pubmed/20446848

73. Nordell AD, McKenna M, Borges AH, Duprez D, Neuhaus J, Neaton JD. Severity of cardiovascular disease outcomes among patients with hiv is related to markers of inflammation and coagulation. J Am Heart Assoc [Internet]. 2014 May 28 [cited 2020 Apr 21];3(3):e000844. Available from: http://www.ncbi.nlm.nih.gov/pubmed/24870935

74. Kwok CS, Kontopantelis E, Kuligowski G, Gray M, Muhyaldeen A, Gale CP, et al. Self-Reported Sleep Duration and Quality and Cardiovascular Disease and Mortality: A Dose-Response Meta- Analysis. J Am Heart Assoc [Internet]. 2018 Aug 7 [cited 2020 Apr 27];7(15). Available from: https://www.ahajournals.org/doi/10.1161/JAHA.118.008552

75. Koren D, Dumin M, Gozal D. Role of sleep quality in the metabolic syndrome. Diabetes Metab Syndr Obes [Internet]. 2016 Aug 25;9:281–310. Available from: https://pubmed.ncbi.nlm.nih.gov/27601926

76. Sokwalla SMR, Joshi MD, Amayo EO, Acharya K, Mecha JO, Mutai KK. Quality of sleep and risk for obstructive sleep apnoea in ambulant individuals with type 2 diabetes mellitus at a tertiary referral hospital in Kenya: A cross-sectional, comparative study. BMC Endocr Disord. 2017;17(1).

77. Brigham EP, Patil SP, Jacobson LP, Margolick JB, Godfrey R, Johnson J, et al. Association between systemic inflammation and obstructive sleep apnea in men with or at risk for HIV infection. Antivir Ther. 2014;19(8):725–33.

78. Cappuccio FP, Miller MA. Sleep and Cardio-Metabolic Disease. Curr Cardiol Rep [Internet]. 2017 Sep 19;19(11):110. Available from: https://pubmed.ncbi.nlm.nih.gov/28929340

79. Miglis MG. Sleep and the Autonomic Nervous System. Sleep Neurol Dis [Internet]. 2017 Jan 1 [cited 2020 Apr 29];227–44. Available from: https://www.sciencedirect.com/science/article/pii/B9780128040744000182?via%3Dihub

80. Breslau N, Roth T, Rosenthal L, Andreski P. Sleep disturbance and psychiatric disorders: A longitudinal epidemiological study of young adults. Biol Psychiatry. 1996 Mar 15;39(6):411–8.

81. Neckelmann D, Mykletun A, Dahl AA. Chronic Insomnia as a Risk Factor for Developing Anxiety and Depression. Sleep [Internet]. 2007 Jul 1;30(7):873–80. Available from: https://doi.org/10.1093/sleep/30.7.873

82. Alvaro PK, Roberts RM, Harris JK. A Systematic Review Assessing Bidirectionality between Sleep Disturbances, Anxiety, and Depression. Sleep [Internet]. 2013 Jul 1 [cited 2020 Apr 21];36(7):1059–68. Available from: https://academic.oup.com/sleep/article/36/7/1059/2453875

83. Nakimuli-Mpungu E, Bass JK, Alexandre P, Mills EJ, Musisi S, Ram M, et al. Depression, alcohol use and adherence to antiretroviral therapy in sub-Saharan Africa: A systematic review [Internet]. Vol. 16, AIDS and Behavior. Springer New York LLC; 2012 [cited 2020 Apr 21]. p. 2101–18. Available from: http://www.ncbi.nlm.nih.gov/pubmed/22116638

84. Brandt C, Zvolensky MJ, Woods SP, Gonzalez A, Safren SA, O'Cleirigh CM. Anxiety symptoms and disorders among adults living with HIV and AIDS: A critical review and integrative synthesis of the empirical literature. Vol. 51, Clinical Psychology Review. Elsevier Inc.; 2017. p. 164–84.

85. Mahmood Z, Hammond A, Nunez RA, Irwin MR, Thames AD. Effects of Sleep Health on Cognitive Function in HIV+ and HIV- Adults. J Int Neuropsychol Soc. 2018 Nov 1;24(10):1038–46.

86. Andrade ASA, Deutsch R, A. Celano S, Duarte NA, Marcotte TD, Umlauf A, et al. Relationships Among Neurocognitive Status, Medication Adherence Measured by Pharmacy Refill Records, and Virologic Suppression in HIV-Infected Persons. JAIDS J Acquir Immune Defic Syndr [Internet]. 2013 Mar 1 [cited 2020 Apr 22];62(3):282–92. Available from: http://journals.lww.com/00126334-201303010-00005

87. Saberi P, Neilands TB, Johnson MO. Quality of Sleep: Associations with Antiretroviral Nonadherence. AIDS Patient Care STDS [Internet]. 2011 Sep 1 [cited 2020 Feb 20];25(9):517–24. Available from: http://www.liebertpub.com/doi/10.1089/apc.2010.0375

88. Babson KA, Heinz AJ, Bonn-Miller MO. HIV Medication Adherence and HIV Symptom Severity: The Roles of Sleep Quality and Memory. AIDS Patient Care STDS [Internet]. 2013 Oct 1 [cited 2020 Feb 25];27(10):544–52. Available from: http://www.liebertpub.com/doi/10.1089/apc.2013.0221

89. Phillips KD, Sowell RL, Boyd M, Dudgeon WD, Hand GA. Sleep quality and health-related quality of life in HIV-infected African-American women of childbearing age. Qual

Life Res [Internet]. 2005 [cited 2020 Feb 25];14(4):959–70. Available from: http://works.bepress.com/kenneth_phillips/16

90. Ibáñez V, Silva J, Cauli O. A survey on sleep questionnaires and diaries. Vol. 42, Sleep Medicine. Elsevier B.V.; 2018. p. 90–6.

91. Smith MT, McCrae CS, Cheung J, Martin JL, Harrod CG, Heald JL, et al. Use of Actigraphy for the Evaluation of Sleep Disorders and Circadian Rhythm Sleep-Wake Disorders: An American Academy of Sleep Medicine Systematic Review, Meta-Analysis, and GRADE Assessment. Vol. 14, Journal of Clinical Sleep Medicine. American Academy of Sleep Medicine; 2018. p. 1209–30.

92. Sadeh A. III. SLEEP ASSESSMENT METHODS. 2015 Mar 1 [cited 2020 Apr 3];80(1):33–48. Available from: http://doi.wiley.com/10.1111/mono.12143

93. Buysse DJ, Reynolds CF, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh sleep quality index: A new instrument for psychiatric practice and research. Psychiatry Res [Internet]. 1989 [cited 2020 Jul 26];28(2):193–213. Available from: https://pubmed.ncbi.nlm.nih.gov/2748771/

94. Chung F, Abdullah HR, Liao P. STOP-bang questionnaire a practical approach to screen for obstructive sleep apnea. Chest [Internet]. 2016 Mar 1 [cited 2020 Jul 18];149(3):631–8. Available from: https://pubmed.ncbi.nlm.nih.gov/26378880/

95. Chiu HY, Chen PY, Chuang LP, Chen NH, Tu YK, Hsieh YJ, et al. Diagnostic accuracy of the Berlin questionnaire, STOP-BANG, STOP, and Epworth sleepiness scale in detecting obstructive sleep apnea: A bivariate meta-analysis [Internet]. Vol. 36, Sleep Medicine Reviews. W.B. Saunders Ltd; 2017 [cited 2020 Jul 18]. p. 57–70. Available from: https://pubmed.ncbi.nlm.nih.gov/27919588/

96. Bosompra N-OA, Orr JE, DeYoung PN, Schmickl CN, Brena R, Gilbertson DC, et al. Validating Sleep Questionnaires in People Living with HIV: Stop-Bang Outperforms the Berlin Questionnaire and Epworth Sleepiness Scale for Identifying Obstructive Sleep Apnea. In: B69 SRN: DIAGNOSIS AND MONITORING OF SLEEP AND SLEEP DISORDERS [Internet]. American Thoracic Society; 2020 [cited 2020 Jul 18]. p. A4155–A4155. Available from: https://www.atsjournals.org/doi/10.1164/ajrccm-conference.2020.201.1_MeetingAbstracts.A4155

97. Monahan PO, Shacham E, Reece M, Kroenke K, Ong'Or WO, Omollo O, et al. Validity/reliability of PHQ-9 and PHQ-2 depression scales among adults living with HIV/AIDS in Western Kenya. J Gen Intern Med. 2009 Feb;24(2):189–97.

98. Chibanda D, Verhey R, Gibson LJ, Munetsi E, Machando D, Rusakaniko S, et al. Validation of screening tools for depression and anxiety disorders in a primary care population with high HIV prevalence in Zimbabwe. J Affect Disord. 2016 Jul 1;198:50–5.

99. Nyongesa MK, Mwangi P, Wanjala SW, Mutua AM, Newton CRJC, Abubakar A. Prevalence and correlates of depressive symptoms among adults living with HIV in rural Kilifi, Kenya. BMC Psychiatry [Internet]. 2019 Nov 1 [cited 2022 Apr 19];19(1):1–10. Available from: https://bmcpsychiatry.biomedcentral.com/articles/10.1186/s12888-019-2339-5

100. Degu F. Sleep Disturbance and Associated Factors among Adult People Living with HIV /

AIDS at Dessie Referral Hospital Antiretroviral therapy clinic ,. 2020 [cited 2020 Dec 24]; Available from: https://doi.org/10.21203/rs.3.rs-34151/v1

101. Johnson DA, Jackson CL, Williams NJ, Alcántara C. Are sleep patterns influenced by race/ethnicity – a marker of relative advantage or disadvantage? Evidence to date. Vol. 11, Nature and Science of Sleep. Dove Medical Press Ltd; 2019. p. 79–95.

102. Grandner MA, Williams NJ, Knutson KL, Roberts D, Jean-Louis G. Sleep disparity, race/ethnicity, and socioeconomic position [Internet]. Vol. 18, Sleep Medicine. Sleep Med; 2016 [cited 2022 Mar 4]. p. 7–18. Available from: https://pubmed.ncbi.nlm.nih.gov/26431755/

103. Jackson CL, Redline S, Emmons KM. Sleep as a potential fundamental contributor to disparities in cardiovascular health [Internet]. Vol. 36, Annual Review of Public Health. Annual Reviews; 2015 [cited 2022 Mar 4]. p. 417–40. Available from: https://www.annualreviews.org/doi/abs/10.1146/annurev-publhealth-031914-122838

104. AO NO. RISK OF OBSTRUCTIVE SLEEP APNEA SYNDROME IN AN ADULT POPULATION WITH HIV INFECTION IN SOUTHWEST NIGERIA. Hypertension. 140(90mmhg):29.

105. Balkissou AD, Pefura-Yone EW, Kengne AP. Prevalence and Risk Factors of Obstructive Sleep Apnea in HIV-Infected Individuals in Yaounde, Cameroon. In: D56 CUDDLE UP A LITTLE CLOSER: SDB NONPULMONARY OVERLAPS [Internet]. American Thoracic Society; 2016. p. A7429–A7429. (American Thoracic Society International Conference Abstracts). Available from: https://doi.org/10.1164/ajrccm-conference.2016.193.1_MeetingAbstracts.A7429

106. Chen YC, Lin CY, Li CY, Zhang Y, Ko WC, Ko NY. Obstructive sleep apnea among HIV-infected men in the highly active antiretroviral therapy era: a nation-wide longitudinal cohort study in Taiwan, 2000–2011. Sleep Med. 2020 Jan 1;65:89–95.

107. Mansoor A-R, Badami VM, Sharma S, Sarwari AR. 922. Increasing incidence of obstructive sleep apnea in patients with HIV: A nationwide database analysis. Open Forum Infect Dis [Internet]. 2020 Dec 31;7(Suppl 1):S495–S495. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7776666/

108. Mengistu N, Belayneh Z, Shumye S. Knowledge, practice and correlates of sleep hygiene among people living with HIV/AIDS attending anti-retroviral therapy at Zewditu Memorial Hospital, Addis Ababa, Ethiopia: a cross-sectional study. Sleep Sci Pract [Internet]. 2020 Dec 16 [cited 2020 Jul 18];4(1):9. Available from: https://sleep.biomedcentral.com/articles/10.1186/s41606-020-00044-0

109. WHO. Depression and Other Common Mental Disorders Global Health Estimates. World Heal Organ [Internet]. 2017 [cited 2022 Apr 19];24. Available from: http://apps.who.int/iris/bitstream/10665/254610/1/WHO-MSD-MER-2017.2-eng.pdf?ua=1

110. Mwangala PN, Mabrouk A, Wagner R, Newton CRJC, Abubakar AA. Mental health and well-being of older adults living with HIV in sub-Saharan Africa: A systematic review. BMJ Open [Internet]. 2021 Sep 22 [cited 2022 Mar 4];11(9). Available from: https://pubmed.ncbi.nlm.nih.gov/34551953/

111. Daubert E, French AL, Burgess HJ, Sharma A, Gustafson D, Cribbs SK, et al. Association of Poor Sleep With Depressive and Anxiety Symptoms by HIV Disease Status: Women's Interagency HIV Study. J Acquir Immune Defic Syndr [Internet]. 2022 Feb 1 [cited 2022 Mar 3];89(2):222–30. Available from: https://journals.lww.com/jaids/Fulltext/2022/02010/Association_of_Poor_Sleep_With_Depressive_and.16.aspx

112. Bedaso A, Abraham Y, Temesgen A, Mekonnen N. Quality of sleep and associated factors among people living with HIV/AIDS attending ART clinic at Hawassa University comprehensive specialized Hospital, Hawassa, SNNPR, Ethiopia. Pakpour AH, editor. PLoS One [Internet]. 2020 Jun 4 [cited 2020 Jul 20];15(6):e0233849. Available from: https://dx.plos.org/10.1371/journal.pone.0233849

113. Abutika RA. Burden of Neuropsychiatric Adverse Effects and Changes in Weight Among Hiv Infected Patients Switched From an Efavirenz Based to a Dolutegravir Based First Line Regimen at the Kenyatta National Hospital. 2020 [cited 2021 Nov 3]; Available from: http://erepository.uonbi.ac.ke/handle/11295/154115

114. Twimukye A, Laker M, Odongpiny EAL, Ajok F, Onen H, Kalule I, et al. Patient experiences of switching from Efavirenz- to Dolutegravir-based antiretroviral therapy: a qualitative study in Uganda. BMC Infect Dis [Internet]. 2021;21(1):1154. Available from: https://doi.org/10.1186/s12879-021-06851-9

115. Angarita GA, Emadi N, Hodges S, Morgan PT. Sleep abnormalities associated with alcohol, cannabis, cocaine, and opiate use: a comprehensive review. Addict Sci Clin Pract 2016 111 [Internet]. 2016 Apr 26 [cited 2022 Apr 20];11(1):1–17. Available from: https://ascpjournal.biomedcentral.com/articles/10.1186/s13722-016-0056-7

116. Abdu Z, Dule A. Poor quality of sleep among HIV-positive persons in Ethiopia. HIV/AIDS - Res Palliat Care [Internet]. 2020 [cited 2022 Mar 5];12:621–8. Available from: /pmc/articles/PMC7588272/

117. Hayashino Y, Yamazaki S, Takegami M, Nakayama T, Sokejima S, Fukuhara S. Association between number of comorbid conditions, depression, and sleep quality using the Pittsburgh Sleep Quality Index: results from a population-based survey. Sleep Med [Internet]. 2010 Apr [cited 2021 Dec 9];11(4):366–71. Available from: https://pubmed.ncbi.nlm.nih.gov/20219425/

118. Framnes SN, Arble DM. The Bidirectional Relationship Between Obstructive Sleep Apnea and Metabolic Disease [Internet]. Vol. 9, Frontiers in Endocrinology . 2018. p. 440. Available from: https://www.frontiersin.org/article/10.3389/fendo.2018.00440

119. Smith SS, Dingwall K, Jorgenson G, Douglas J. Associations between the use of common medications and sleep architecture in patients with untreated obstructive sleep apnea. J Clin sleep Med JCSM Off Publ Am Acad Sleep Med. 2006 Apr;2(2):156–62.

120. Krishnan V, Dixon-Williams S, Thornton JD. Where There Is Smoke…There Is Sleep Apnea: Exploring the Relationship Between Smoking and Sleep Apnea. Chest [Internet]. 2014 Dec 1 [cited 2022 Apr 17];146(6):1673. Available from: /pmc/articles/PMC4251622/

121. Taveira KVM, Kuntze MM, Berretta F, de Souza BDM, Godolfim LR, Demathe T, et al.

Association between obstructive sleep apnea and alcohol, caffeine and tobacco: A meta-analysis [Internet]. Vol. 45, Journal of Oral Rehabilitation. John Wiley & Sons, Ltd; 2018 [cited 2022 Mar 7]. p. 890–902. Available from: https://onlinelibrary.wiley.com/doi/full/10.1111/joor.12686

122. Charokopos N, Leotsinidis M, Tsiamita M, Karkoulias K, Spiropoulos K. Sleep apnea syndrome in a referral population in Greece: influence of social factors. Lung [Internet]. 2007 Aug [cited 2022 Apr 18];185(4):235–40. Available from: https://pubmed.ncbi.nlm.nih.gov/17564744/

123. Gallus S, Odone A, Lugo A, Bosetti C, Colombo P, Zuccaro P, et al. Overweight and obesity prevalence and determinants in Italy: an update to 2010. Eur J Nutr 2012 522 [Internet]. 2012 May 27 [cited 2022 Apr 18];52(2):677–85. Available from: https://link.springer.com/article/10.1007/s00394-012-0372-y

124. Guglielmi O, Lanteri P, Garbarino S. Association between socioeconomic status, belonging to an ethnic minority and obstructive sleep apnea: a systematic review of the literature. Sleep Med. 2019 May 1;57:100–6.

125. Mukora-Mutseyekwa F, Zeeb H, Nengomasha L, Adjei NK. Trends in Prevalence and Related Risk Factors of Overweight and Obesity among Women of Reproductive Age in Zimbabwe, 2005–2015. Int J Environ Res Public Heal 2019, Vol 16, Page 2758 [Internet]. 2019 Aug 2 [cited 2022 Apr 18];16(15):2758. Available from: https://www.mdpi.com/1660-4601/16/15/2758/htm

126. Asgari S, Najafi A, Sadeghniiat K, Gholamypour Z, Akbarpour S. The association between body mass index and risk of obstructive sleep apnea among patients with HIV. J Res Med Sci [Internet]. 2021 [cited 2022 Apr 16];26(1):123. Available from: https://www.jmsjournal.net/article.asp?issn=1735-1995;year=2021;volume=26;issue=1;spage=123;epage=123;aulast=Asgari

127. Mafort TT, Rufino R, Costa CH, Lopes AJ. Obesity: Systemic and pulmonary complications, biochemical abnormalities, and impairment of lung function. Multidiscip Respir Med [Internet]. 2016 Jul 12 [cited 2022 Apr 15];11(1):1–11. Available from: https://mrmjournal.biomedcentral.com/articles/10.1186/s40248-016-0066-z

128. Onat A, Hergenç G, Yüksel H, Can G, Ayhan E, Kaya Z, et al. Neck circumference as a measure of central obesity: associations with metabolic syndrome and obstructive sleep apnea syndrome beyond waist circumference. Clin Nutr [Internet]. 2009 Feb [cited 2022 Apr 15];28(1):46–51. Available from: https://pubmed.ncbi.nlm.nih.gov/19010573/

129. Lin CM, Davidson TM, Ancoli-Israel S. Gender differences in obstructive sleep apnea and treatment implications. Sleep Med Rev. 2008 Dec 1;12(6):481–96.

130. Abdeen Y, Al-Halawani M, Kaako A, Hao I, Dazley J, Katpally R, et al. Effect of the duration of protease inhibitor therapy in HIV-infected individuals on the severity of obstructive sleep apnea. J Res Med Sci [Internet]. 2019 Jan 1 [cited 2022 Apr 17];24(1). Available from: /pmc/articles/PMC6669999/

131. Eckard AR, McComsey GA. Weight Gain and Integrase Inhibitors. Curr Opin Infect Dis [Internet]. 2020 Feb 1 [cited 2022 Apr 17];33(1):10. Available from: /pmc/articles/PMC7433018/

132. Bailin SS, Gabriel CL, Wanjalla CN, Koethe JR. Obesity and Weight Gain in Persons with HIV. Curr HIV/AIDS Rep [Internet]. 2020 Feb 18 [cited 2022 Apr 17];17(2):138–50. Available from: https://link.springer.com/article/10.1007/s11904-020-00483-5

APPENDICES

Appendix 1: Screening proforma

Study No.: …….

1. Age: …….
2. Date of Birth: ……
3. Gender: Female ☐ (1) Male ☐ (2)
4. Are you pregnant? Yes (1) ☐ No (2) ☐
5. Have you given birth within the last 6 weeks? Yes ☐ (1) No ☐ (2)
6. Are you on any anxiolytic, antidepressant, mood stabilizing, antipsychotic, or antiepileptic drugs? Yes (1) ☐ No (2) ☐
7. Are you willing to participate in the study to assess quality of sleep and burden of sleep disturbances among HIV infected patients at the KNH CCC?

   ☐ YES (1)

   ☐ NO (2)

Appendix 2: Participant information and consent form

QUALITY OF SLEEP AND RISK OF OBSTRUCTIVE SLEEP APNEA IN ADULTS WITH HIV INFECTION AT KENYATTA NATIONAL HOSPITAL

Principal Investigator

Dr. Mutai Ebby Chelangat - **UoN**

Co-Investigators

Dr. Jared O. Mecha- **UoN**

Prof. Erastus O. Amayo - **UoN**

Introduction:

I would like to tell you about a study being conducted by the above listed researchers. The purpose of this consent form is to give you the information you will need to help you decide whether or not to be a participant in the study. Feel free to ask any questions about the purpose of the research, what happens if you participate in the study, the possible risks and benefits, your rights as a volunteer, and anything else about the research or this form that is not clear. When we have answered all your questions to your satisfaction, you may decide to be in the study or not. This process is called 'informed consent'. Once you understand and agree to be in the study, I will request you to sign your name on this form. You should understand the general principles which apply to all participants in medical research:

i) Your decision to participate is entirely voluntary.

ii) You may withdraw from the study at any time without necessarily giving a reason for your withdrawal.

iii) Refusal to participate in the research will not affect the services you are entitled to in this health facility or other facilities.

We will give you a copy of this form for your records.

May I continue?

YES ☐ NO ☐

This study has approval by The Kenyatta National Hospital-University of Nairobi Ethics and Research Committee Protocol No. _____

What is the study about?

Sleep disorders occur more commonly among people living with HIV. This study aims to quantify the prevalence of poor quality of sleep and to assess risk for obstructive sleep apnea among patients living with HIV. Recommendations from the study results can be made to the administration to improve screening and management of sleep disorders among people living with HIV.

Study Procedure

The study procedure involves reviewing and abstracting data from your electronic medical records. The data of interest includes: bio data, treatment regimen (previous and current), CD4 count, and viral load. Furthermore, a brief physical exam will be conducted to measure your weight, height and neck circumference using a weighing scale, stadiometer and tape measure respectively. We will also ask you questions from four brief questionnaires that will help us gather further information critical to the study. This whole process will tentatively take 30 minutes or less of your time.

Benefits of the study

Knowledge from the study findings will help improve future care of people living with HIV. The improved care will reduce HIV related mortality and morbidity associated with sleep disturbances. Participants shall not receive any monetary compensation to take part in the study.

Risks of the study

Your participation in this study has minimal risk. You might feel some discomfort when answering questions about your personal life**.**

Confidentiality

All the information provided will remain strictly confidential. The filled study proforma, questionnaires and signed consent forms will bear unique codes and will be kept in a lockable cabinet which will be accessed by the principal investigator only.

Participation

Participation in this study is on voluntary basis and you are allowed to withdraw at any point or decline to participate without any victimization.

Participant's statement

I have read this consent form or had the information read to me. I have had my questions answered in a language that I understand. The risks and benefits have been explained to me. I understand that my participation in this study is voluntary and that I may choose to withdraw at any time. I freely agree to participate in this research study.

I understand that all efforts will be made to keep information regarding my personal identity confidential. By signing this consent form, I have not given up any of the legal rights that I have as a participant in a research study.

I agree to participate in this research study: **Yes** **No**

Participant signature / Thumb stamp

Date__

Researcher's statement

I, the undersigned, have fully explained the relevant details of this research study to the participant named above and believe that the participant has understood and has willingly and freely given his/her consent.

Researcher's Name **Date**

Signature:

Questions about the research

If you have any questions on the study, kindly contact me (principal investigator) on this telephone number 0750770177.

For more information about your rights as a research participant you may contact the Secretary/Chairperson, Kenyatta National Hospital-University of Nairobi Ethics and Research Committee Telephone No. 2726300 Ext. 44102. Email: uonknh_erc@uonbi.ac.ke

Appendix 3: Ridhaa ya Kiswahili

UBORA WA USINGIZI NA HATARI YA UGONJWA WA KUKOSA PUMZI USINGIZINI KWA WATU WAZIMA WALIO NA AMBUKIZO LA VIRUSI VYA UKIMWI (VVU) KATIKA HOSPITALI YA KITAIFA YA KENYATTA.

Mtafiti mkuu

Dr. Mutai Ebby Chelangat - **UoN**

Watafiti wenza

Dr. Jared. O. Mecha- **UoN**

Prof. Erastus Amayo - **UoN**

Utangulizi:

Ningependa kukufahamisha kuhusu utafiti huu unaofanywa na watafiti ambao wametajwa hapo juu. Umuhimu wa fomu hii ni kukujulisha yale unatakiwa kujua kabla ya kuamua kushiriki au kutoshiriki katika utafiti huu. Unaweza kuuliza maswali yoyote kuhusu umuhimu wa utafiti huu, faida na hasara zake kama zipo, haki zako ikiwa utajitolea kushiriki na chochote ambacho hujaelewa.

Utakapoelewa utahitajika kutia sahihi kwenye fomu hii.

Unapaswa kuelewa kuwa;

i. Haifai kulazimishwa kushiriki ila kwa uamuzi wako mwenyewe.

ii. Unaweza kujitoa kwenye utafiti huu wakati wowote ule bila kutoa sababu.

iii. Matibabu yako yataendelea kama kawaida hata utakapo kataa kushiriki katika utafiti huu.

Tutakupatia fomu nyingine ili uweze kuiweka.

Je, niendelee?

Ndio La

Utafiti huu umeidhinishwa na KNH-university ya Nairobi ethics &Research committee protocol no. ___

Utafiti huu unahusu nini?

Magonjwa za kulala hujitokeza zaidi miongoni mwa watu walio na virusi vya ukimwi (VVU). Utafiti huu unakusudia kujumlisha idadi ya watu wazima walio na ambukizo la VVU walio na ubora duni wa usingizi, na pia kutathmini hatari ya ugonjwa wa kukosa pumzi kwa muda ukiwa usingizini. Mapendekezo kutoka kwa matokeo ya utafiti huu yanaweza kutumika na wasimamizi kwa kuboresha uchunguzi na matibabu ya shida za kulala kati ya watu wenye VVU.

Utaratibu wa utafiti

Utaratibu wa utafiti utahusu kupitia rekodi zako za matibabu ili kujua madawa unazotumia, hesabu za CD4, viral load. Mtihani mfupi wa kimwili wa kupima uzito, urefu, na mzunguko wa shingo utafanywa. Pia tutakuuliza maswali kutoka kwa fomu nne fupi. Jina lako halitatajwa katika profoma ya utafiti. Haya yote yatachukua muda wa dakika kama thelathini (30).

Faida ya utafiti

Maarifa yatakayotokana na utafiti huu yataboresha matibabu ya wagonjwa siku zijazo. Washiriki hawatapata faida yoyote ya kifedha kwa kushiriki katika utafiti huu.

Hatari ya utafiti

Ushiriki wako katika utafiti huu una hatari chache. Utaweza kuhisi kwamba unasumbuliwa utakapokua unajibu maswali kuhusu maisha yako ya kibinafsi**.**

Usiri

Habari zote utakazotoa zitabaki kuwa siri. Fomu zitakazotumika kwenya utafiti huu zitabeba nambari za kipekee na zitahifadhiwa kwenye kabati maalum linaloweza kufikiwa tu na mtafiti mkuu.

Kushiriki

Kushiriki kwa utafiti huu ni kwa hiari na uko na uhuru wa kujitoa katika hatua yoyote ama kukataa kushiriki bila ya maonevu.

Fomu ya idhini

Nimesoma fomu hii. Nimepata fursa ya kujadili utafitii huu. Maswali yangu yamejibiwa kwa lugha ninayoielewa. Nimeelewa faida na hatari zinazotokana na utafiti huu. Nimeelewa kuwa kushiriki kwangu sio kwa lazima na ninaweza kujitoa wakati wowote ule.

Nakubali kushiriki kwenye utafiti huu. Naelewa kua juhudi zimewekwa kuhakikisha habari nitakazozitoa zitakua ni siri.

Kwa kutia sahihi sijapoteza haki zangu kama muhusika.

Nakubali kushiriki katika utafiti huu **Ndio** **La**

Sahihi ya mshirika /alama ya kidole_____

Tarehe ……

Kauli ya mtafiti

Mimi niliyetia sahihi kwenye karatasi hii nimeeleza kwa kina mambo yote ambayo mshiriki aliyetajwa hapo juu anapaswa kuelewa na amekubali kushiriki katika utafiti huu bila kulazimishwa.

Jina la mtafiti_____ Tarehe_____

Sahihi:

Jukumu kwenye utafiti_____

Maswali kuhusu utafiti

Kama una maswali yoyote tafadhali wasiliana nami kwa nambari hii ya simu: 0750770177.

Iwapo kuna maswali zaidi kuhusu haki zako kama mshiriki kwenye utafiti huu, wasiliana na karani/mwenyekiti KNH- Chuo Kikuu cha Nairobi Ethics &Research Committee, nambari ya simu: 2726300 Ext 44102. Barua pepe: email uonknh_erc@uonbi.ac.ke.

Appendix 4: Study Proforma

SECTION I:

Patient number: _____

Study number: _____

A. Sociodemographic data

1. Age (years): _____
2. Gender:
   Male (1) ☐ Female (2) ☐
3. Highest level of education achieved:

   None at all (1) ☐

   Primary level (2) ☐

   Secondary level (3) ☐

   Tertiary level (4) ☐
4. Marital status:

   Single (1) ☐ Married (2) ☐ Divorced (3) ☐

   Widowed (4) ☐ Separated (5) ☐
5. Employment status: Formal employment (1) ☐ Not employed (2) ☐

6. Use of alcohol: Yes (1) ☐ No (2) ☐
7. Use of cigarettes: Yes (1) ☐ No (2) ☐
8. Use of khat: Yes (1) ☐ No (2) ☐
9. Use of any other recreational drugs (injectable or other): Yes (1) ☐ No (2) ☐

   If yes, specify which: _____

B. Clinical data

1. Time since HIV diagnosis (years) _____
2. Time since first ever initiation of antiretroviral therapy (in years) _____
3. Nadir CD4 count _____
4. Current viral load (within 6 months) _____copies/ml
5. Viral load <1000 copies/ml: Yes (1) ☐ No (2) ☐
6. Current WHO (World Health Organization) Stage:

   Stage 1☐ Stage 2☐ Stage 3 ☐ Stage 4 ☐

7. Current antiretroviral therapy regimen (specify type) _____
8. *Duration of use of this antiretroviral therapy regimen*_____
9. Current antiretroviral therapy regimen: First line ☐ Second line ☐

   Third line ☐ Other ☐

10. History of change of antiretroviral therapy regimen: Yes (1) ☐ No (2) ☐
11. Reason for change of regimen: Optimized (1) ☐ Failed (2) ☐
    Adverse drug reaction (3) ☐ Comorbid condition (4) ☐
12. Known co-morbidity (specify) _____
13. Additional medications _____
14. History of hospitalization: Yes (1) ☐ No (2) ☐
15. If yes, number of hospitalizations _____
16. Weight =
17. Height =
18. BMI =
19. Neck circumference =

SECTION II: ASSESSMENT OF ANXIETY

Generalized Anxiety Disorder Questionnaire (GAD-7)

Over the last two weeks, how often have you been bothered by the following problems?	**Not at all**	**Several days**	**More than half the days**	**Nearly every day**
1. Feeling nervous, anxious, or on edge	0	1	2	3
2. Not being able to stop or control worrying	0	1	2	3
3. Worrying too much about different things	0	1	2	3
4. Trouble relaxing	0	1	2	3
5. Being so restless that it is hard to sit still	0	1	2	3
6. Becoming easily annoyed or irritable	0	1	2	3
7. Feeling afraid, as if something awful might happen	0	1	2	3

Column totals _____ + _____ + _____ +_____

***Total score* = _____**

Scoring GAD-7 Anxiety Severity
This is calculated by assigning scores of 0, 1, 2, and 3 to the response categories, respectively, of "not at all," "several days," "more than half the days," and "nearly every day."
GAD-7 total score for the seven items ranges from 0 to 21.

0–4: minimal anxiety

5–9: mild anxiety

10–14: moderate anxiety

15–21: severe anxiety

Anxiety score:

a) Anxiety present (score ≥5) (1) ☐ b) Anxiety absent (score <5) (2) ☐

SECTION III: ASSESSMENT OF DEPRESSION

Patient Health Questionnaire (PHQ-9)

Patient Health Questionnaire (PHQ-9)				
Over the last 2 weeks, how often have you been bothered by any of the following problems?	**Not at all**	**Several days**	**More than half the days**	**Nearly every day**
1. Little interest or pleasure in doing things				
2. Feeling down, depressed, or hopeless				
3. Trouble falling or staying asleep, or sleeping too much.				
4. Feeling tired or having little energy. . . .				
5. Poor appetite or overeating.....				
6. Feeling bad about yourself or that you are a failure or have let yourself or your family down				
7. Trouble concentrating on things, such as reading the newspaper or watching television				
8. Moving or speaking so slowly that other people could have noticed? Or the opposite—being so fidgety or restless that you have been moving around a lot more than usual.				
9. Thoughts that you would be better off dead or of hurting yourself in some way				

Scoring and Interpretation:

Count the number (#) of boxes checked in a column. Multiply that number by the value indicated below, then add the subtotal to produce a total score. The possible range is 0-27. Use the table below to interpret the PHQ-9 score.

Not at all (#) _____ x 0 = _____ Several days (#) _____ x 1 = _____

More than half the days (#) _____ x 2 = _____ Nearly every day (#) _____ x 3 = _____

Total score: _____

Diagnosis

0-4 = Minimal depression, 5-9 = Mild depression, 10-14 = Moderate depression,
15-19 = Moderately severe depression, 20-27 = Severe depression

Depression score:

a) Depression present (score ≥5) (1) ☐ b) Depression absent (score <5) (2) ☐

SECTION IV: ASSESSMENT OF SLEEP QUALITY
Pittsburgh Sleep Quality Index

Name:_____ Date: _____

Pittsburgh Sleep Quality Index (PSQI)

Instructions: The following questions relate to your usual sleep habits during the past month only. Your answers should indicate the most accurate reply for the majority of days and nights in the past month. **Please answer all questions.**

1. During the past month, what time have you usually gone to bed at night? _____
2. During the past month, how long (in minutes) has it usually taken you to fall asleep each night? _____
3. During the past month, what time have you usually gotten up in the morning? _____
4. During the past month, how many hours of actual sleep did you get at night? (This may be different than the number of hours you spent in bed.) _____

5. During the past month, how often have you had trouble sleeping because you…	Not during the past month	Less than once a week	Once or twice a week	Three or more times a week
a. Cannot get to sleep within 30 minutes				
b. Wake up in the middle of the night or early morning				
c. Have to get up to use the bathroom				
d. Cannot breathe comfortably				
e. Cough or snore loudly				
f. Feel too cold				
g. Feel too hot				
h. Have bad dreams				
i. Have pain				
j. Other reason(s), please describe:				
6. During the past month, how often have you taken medicine to help you sleep (prescribed or "over the counter")?				
7. During the past month, how often have you had trouble staying awake while driving, eating meals, or engaging in social activity?				
	No problem at all	Only a very slight problem	Somewhat of a problem	A very big problem
8. During the past month, how much of a problem has it been for you to keep up enough enthusiasm to get things done?				
	Very good	Fairly good	Fairly bad	Very bad
9. During the past month, how would you rate your sleep quality overall?				

	No bed partner or room mate	Partner/room mate in other room	Partner in same room but not same bed	Partner in same bed
10. Do you have a bed partner or room mate?				
	Not during the past month	Less than once a week	Once or twice a week	Three or more times a week
If you have a room mate or bed partner, ask him/her how often in the past month you have had:				
a. Loud snoring				
b. Long pauses between breaths while asleep				
c. Legs twitching or jerking while you sleep				
d. Episodes of disorientation or confusion during sleep				
e. Other restlessness while you sleep, please describe:				

Sleep quality score:

a) Poor sleep quality (score >5) (1) ☐

b) Good sleep quality (score ≤5) (2) ☐

Scoring the PSQI

The order of the PSQI items has been modified from the original order in order to fit the first 9 items (which are the only items that contribute to the total score) on a single page. Item 10, which is the second page of the scale, does not contribute to the PSQI score.

In scoring the PSQI, seven component scores are derived, each scored 0 (no difficulty) to 3 (severe difficulty). The component scores are summed to produce a global score (range 0 to 21). Higher scores indicate worse sleep quality.

Component 1: Subjective sleep quality—question 9

Response to Q9	Component 1 score
Very good	0
Fairly good	1
Fairly bad	2
Very bad	3

Component 1 score:_____

Component 2: Sleep latency—questions 2 and 5a

Response to Q2	Component 2/Q2 subscore
≤ 15 minutes	0
16-30 minutes	1
31-60 minutes	2
> 60 minutes	3

Response to Q5a	Component 2/Q5a subscore
Not during past month	0
Less than once a week	1
Once or twice a week	2
Three or more times a week	3

Sum of Q2 and Q5a subscores	Component 2 score
0	0
1-2	1
3-4	2
5-6	3

Component 2 score:_____

Component 3: Sleep duration—question 4

Response to Q4	Component 3 score
> 7 hours	0
6-7 hours	1
5-6 hours	2
< 5 hours	3

Component 3 score:_____

Component 4: Sleep efficiency—questions 1, 3, and 4

Sleep efficiency = (# hours slept/# hours in bed) X 100%

hours slept—question 4

hours in bed—calculated from responses to questions 1 and 3

Sleep efficiency	Component 4 score
> 85%	0
75-84%	1
65-74%	2
< 65%	3

Component 4 score:_____

Component 5: Sleep disturbance—questions 5b-5j

Questions 5b to 5j should be scored as follows:

Not during past month	0
Less than once a week	1
Once or twice a week	2
Three or more times a week	3

Sum of 5b to 5j scores	Component 5 score
0	0
1-9	1
10-18	2
19-27	3

Component 5 score:_____

Component 6: Use of sleep medication—question 6

Response to Q6	Component 6 score
Not during past month	0
Less than once a week	1
Once or twice a week	2
Three or more times a week	3

Component 6 score:_____

Component 7: Daytime dysfunction—questions 7 and 8

Response to Q7	Component 7/Q7 subscore
Not during past month	0
Less than once a week	1
Once or twice a week	2
Three or more times a week	3

Response to Q8	Component 7/Q8 subscore
No problem at all	0
Only a very slight problem	1
Somewhat of a problem	2
A very big problem	3

Sum of Q7 and Q8 subscores	Component 7 score
0	0
1-2	1
3-4	2
5-6	3

Component 7 score:_____

Global PSQI Score: Sum of seven component scores:_____

Citation: Buysse, DJ, Reynolds CF, Monk TH, Berman SR, Kupfer DJ: The Pittsburgh Sleep Quality Index (PSQI): A new instrument for psychiatric research and practice. Psychiatry Research 28:193-213, 1989

SECTION V: ASSESSMENT OF RISK OF OBSTRUCTIVE SLEEP APNEA (OSA)
Stop-Bang Sleep Apnea Questionnaire

STOP		
1. Do you **S**NORE loudly (louder than talking or loud enough to be heard through closed	Yes	No
2. Do you often feel **T**IRED, fatigued, or sleepy during daytime?	Yes	No
3. Has anyone **O**BSERVED you stop breathing during your sleep?	Yes	No
4. Do you have or are you being treated for high blood	Yes	No

BANG		
5. **B**MI more than 35kg/m2?	Yes	No
6. **A**GE over 50 years old?	Yes	No
7. **N**ECK circumference > 16 inches (40cm)?	Yes	No
8. **G**ENDER: Male?	Yes	No

TOTAL SCORE		

- High risk of obstructive sleep apnea: Yes to 5 – 8 questions, or

  a score of ≥2 + male gender,
  or a score of ≥2 + BMI > 35kg/m^2
  or a score of ≥2 or more of 4 STOP questions + neck circumference 16 inches / 40cm.

- Intermediate risk of obstructive sleep apnea: Yes to 3 – 4 questions
- Low risk of obstructive sleep apnea: Yes to 0 – 2 questions

Risk for obstructive sleep apnea (OSA):

a) High risk (score > 5) (1) ☐ b) Low risk (score ≤2) (2) ☐

Appendix 5: Proforma ya Utafiti

SEHEMU YA I:

Nambari ya mgonjwa: __

Nambari ya kujifunza: __

Data ya sociodemographic

1. Umri (miaka): __
2. Jinsia:
   Mwanamume (1) ☐ Mwanamke (2) ☐
3. Kiwango cha juu cha elimu kupatikana:
   a. Hakuna hata mmoja (1) ☐
   b. Kiwango cha msingi (2) ☐
   c. Ngazi ya sekondari (3) ☐
   d. Kiwango cha juu (4) ☐
4. Hali ya ndoa:
   Pekee (1) ☐ Mshirika (2) ☐ Mjane (3) ☐
   Mjane (4) ☐ Tulitengana (5) ☐
5. Hali ya ajira: Walioajiriwa (1) ☐ Hawakuajiriwa (2) ☐
6. Matumizi ya pombe: Ndiyo (1) ☐ Hapana (2) ☐
7. Matumizi ya sigara: Ndiyo (1) ☐ Hapana (2) ☐
8. Matumizi ya khat: Ndiyo (1) ☐ Hapana (2) ☐
9. Matumizi ya dawa nyingine yoyote ya burudani (sindano au nyingine):

Ndiyo (1) ☐ Hapana (2) ☐

Ikiwa ndiyo, taja aina / jina: __

Data ya kliniki

1. Muda tangu utambuzi wa VVU (miaka) __
2. Mara ya kwanza tangu mwanzo wa ART (miaka) __

3. Nadir CD4 count __
4. Kiwango cha virusi (katika miezi 6 iliyopita) _____copies / mililita
5. Kiwango < 1000 / ml: Ndiyo (1) ☐ Hapana (2) ☐
6. Hatua ya sasa ya WHO (World Health Organization):

   Hatua ya 1 ☐ Hatua ya 2 ☐ Hatua ya 3 ☐ Hatua ya 4 ☐

7. Aina ya dawa ya kupambana na virusi vya ukimwi (ART) unayotumia kwa sasa (taja aina) __
8. *Muda wa matumizi ya aina hii ya ART__*
9. Mstari wa sasa wa aina ya ART:

   Mstari wa kwanza ☐ Mstari wa pili ☐ Mstari wa tatu ☐

   Aina ingine ☐

10. Historia ya kubadilishwa kwa aina ya ART: Ndiyo (1) ☐ Hapana (2) ☐
11. Sababu ya kubadilishwa kwa aina ya ART: Optimised (1) ☐ Imeshindikana (2) ☐

    Athari mbaya ya madawa (3) ☐ Kuwepo kwa magonwa mengine (4) ☐

12. Magonjwa mengine (taja) __
13. Dawa za ziada __
14. Historia ya kulazwa hospitalini: Ndiyo (1) ☐ Hapana (2) ☐
15. Kama ndiyo, idadi ya kulazwa hospitalini __
16. Uzito =
17. Urefu =
18. BMI =
19. Mzunguko wa shingo =

SEHEMU YA II: TATHMINI YA WASIWASI

Generalized Anxiety Disorder Questionnaire (GAD-7) – Swahili Version

Katika wiki mbili zilizopita, ni mara ngapi umekuwa ukisumbuliwa na shida zifuatazo?	**Hakuna kabisa**	**Siku kadhaa**	**Zaidi ya nusu ya siku hizi**	**Karibu kila siku**
1. Kuwa na dukuduku, au kuhisi wasiwasi	0	1	2	3
2. Kutokuwa na uwezo wa kuacha au kudhibiti hali ya kuwa na wasiwasi	0	1	2	3
3. Kuwa na wasiwasi sana juu ya vitu tofauti	0	1	2	3
4. Kuwa na shida kupumzika	0	1	2	3
5. Kuhangaika hadi ni ngumu kukaa kwa utulivu	0	1	2	3
6. Kukasirika au kutukuta kwa urahisi	0	1	2	3
7. Kuhisi hofu kana kwamba kunaweza kutokea kitu mbaya	0	1	2	3

Jumla _____ + _____ + _____ + _____

***Jumla ya alama* = _____**

SEHEMU YA III: TATHMINI YA MSONGO WA MAWAZO

Patient Health Questionnaire (PHQ-9) – Swahili Version

Kidodosi juu ya afya ya Mgonjwa				
Kwa kipindi cha wiki mbili zilizopita, ni mara ngapi umesumbuliwa na matatizo haya yafuatayo? (Weka alama kuonyesha jibu lako)	**Hapana kabisa**	**siku kadhaa**	**Zaidi ya nusu ya siku hizi**	**karibu kila siku**
1. Mwelekeo mdogo au kukosa raha wa kufanya vitu				
2. Kujisikia kama huwezi kuchangamka, kusikia, huzuni au kukosa tumaini				
3. Tatizo kupata usingizi au tatizo kuendelea kulala baada ya usingizi, amakulalakupitakiasi				
4. Kujisikia kuchoka au kuwa na nguvu kidogo				
5. Hama ya kula ni mbaya, au kula kupita kiasi				
6. Kusikia vibaya kuhusu binafsi, au kuskia kama umeshindwa, au umejishusha, ama umeshusha chini familia yako				
7. Tatizo kutuliza akili kwenye vitu kama kusoma gazeti au kusilikiliza radio				
8. Kusogea au kuzungumza pole pole sana hata ingeweza kuonekana kwa watu wengine. Ama kinyume-kuwa na mashaka/wasiwasi au kutotulia kiasi hata umekuwa ukitembea tembea sanakulikokawaida				
9. Fikira kwamba ni heri ukifa, au fikira za kujiumiza kawa njia fulani				

SEHEMU YA IV: TATHMINI YA UBORA WA USINGIZI

PITTSBURGH SLEEP QUALITY INDEX- MDODOSO (KISWAHILI)

Jina: _____ Tarehe: _____

Maelekezo: Maswali yafuatayo yanahusiana na tabia yako ya kawaida ya usingizi katika mwezi uliopita tu. Majibu yako yanahitaji kuonyesha jibu **sahihi zaidi** kwa wingi wa mchana na usiku katika mwezi uliopita. Tafadhali jibu maswali yote.

1. Katika mwezi uliopita, huwa unaingia kitandani usiku saa ngapi kwa kawaida?_____
2. Katika mwezi uliopita, kwa kawaida huwa inakuchukua muda gani (kwa dakika) kupata usingizi kila usiku? _____
3. Katika mwezi uliopita, kwa kawaida huwa unaamka asubuhi saa ngapi? _____
4. Katika mwezi uliopita, ni masaa mangapi halisi ulilala kila usiku? (Hii inaweza kuwa tofauti na idadi ya masaa uliokuwa kitandani). _____

5.Katika mwezi uliopita, ni mara ngapi umepata shida kulala kwa sababu:	Sikuwa na shida kwa mwezi uliopita	Si zaidi ya mara moja kwa wiki	Mara moja au mbili kwa wiki	Mara tatu au zaidi kwa wiki
a. Hukuweza kupata usingizi katika dakika 30 za kwanza				
b. Uliamka katikati ya usiku au asubuhi mapema				
c. Ulihitaji kuamka kutumia msalalani/ choo				
d. Hukuweza kupumua vizuri				
e. Ulikohoa au kukoroma kwa sauti kubwa.				
f. Ulihisi baridi sana				
g. Ulihisi joto sana.				
h. Ulipata ndoto mbaya.				
i. Ulihisi uchungu.				
j. Sababu zingine (tafadhali eleza zaidi):				
6. Katika mwezi uliopita, ni mara ngapi umetumia dawa za kukusaidia kulala (ilioagizwa na daktari au bila kuagizwa)?				
7. Katika mwezi uliopita, ni mara ngapi ulipata shida kukaa macho wakati wa kuendesha gari au kukula chakula au kufanya shuguli zako?				
	Sikuwa na tatizo lolote	Tatizo kidogo tu	Tatizo kiasi	Tatizo kubwa sana
8. Katika mwezi uliopita, ulikuwa na kiasi gani cha tatizo la hamu ya kutenda shughuli zako?				
	Mzuri sana	Mzuri kiasi	Mbaya kiasi	Mbaya sana
9. Katika mwezi uliopita, utapimaje kiwango/ubora wa usingizi wako kwa jumla?				
	Hapana	Yuko lakini hulala katika chumba kingine	Yuko Chumbani mwangu lakini hulala katika kitanda	Kitandani mwangu

			kingine	
10. Je, unatumia kitanda kimoja au chumba kimoja na mtu mwingine?				
	Sikuwa na shida kwa mwezi uliopita	Si zaidi ya mara moja kwa wiki	Mara moja au mbili kwa wiki	Mara tatu au zaidi kwa wiki
Ikiwa una mwenzako kwa kitanda kimoja au kwa chumba kimoja, muulize ni mara ngapi katika mwezi ulliopita ulikuwa na:				
a. Mkoromo kwa sauti kubwa				
b. Misimamo mrefu (kuacha kupumua)katika pumzi katika usingizi/				
c. Miguu kupapatika au kutetemeka katika usingizi.				
d. Nyakati za kuchanganyikiwa unapoamka katikati ya usingizi.				
e. Nyakati za kutotulia kwa sababu zingine wakati ulipokuwa umelala, tafadhali eleza:				

SEHEMU YA V: STOP-BANG SLEEP APNEA QUESTIONNAIRE (SWAHILI VERSION)

"STOP"		
Je, unakoroma kwa sauti kubwa (sauti zaidi kuliko ya kuongea au sauti kubwa kusikika kupitia milango iliyofungwa)?	Yes	No
Je, wewe huhisi kwa mara nyingi, uchovu, au kulala wakati wa mchana?	Yes	No
Je, kuna yeyote ameshuhudia kuacha kupumua kwako wakati wa kulala?	Yes	No

"BANG"		
Fahirisi ya misa ya mwili zaidi ya 35kg/m2?	Yes	No
Umri zaidi ya miaka 50?	Yes	No
Mzunguko wa shingo > inchi 16 (40cm)?	Yes	No
JINSIA: Kiume?	Yes	No

JUMLA YA ALAMA		

Appendix 6: Time frame

Table 18: Schedule of planned activities

	Oct. 2020–Feb 2021	March	April	May	June	July	August	Sept.	October 2021
Proposal development									
Protocol presentation									
Ethical approval									
Data collection									
Data analysis									
Results presentation									

Appendix 7: Budget estimation and justification

Table 19:Budget estimation

Item	Quantity	Cost
Training and remuneration of research assistants	2	40,000
Statistician's allowance	1	30,000
Stationery and printing	Questionnaires and protocol drafts	30,000
Ethics committee review fees		2,000
Transport		30,000
Contingency		20,000
Total		152,000

The two research assistants were involved in the recruitment and data collection procedures of the study in association with the principal investigator.

The statistician had expertise in data analysis thus ensured appropriate interpretation of collected data. Both the research assistants and the statistician were paid on contract basis.

The PI funded the entire study.

Appendix 8: Ethical Approval

UNIVERSITY OF NAIROBI
COLLEGE OF HEALTH SCIENCES
P O BOX [illegible]
Telegrams: varsity
Tel [illegible]

KNH-UON ERC
Email: [illegible]
Website: [illegible]
Facebook: [illegible]
Twitter: [illegible]

KENYATTA NATIONAL HOSPITAL
P O BOX [illegible]
Tel: [illegible]
Fax: 725070
Telegrams: MEDSUP, Nairobi

Ref: KNH-ERC/A/294

16th August, 2021

Dr. Ebby Chelangat Mutai
Reg. No.H58/8771/2017
Dept. of Clinical Medicine and Therapeutics
School of Medicine
College of Health Sciences
University of Nairobi

Dear Dr. Mutai

RESEARCH PROPOSAL: QUALITY OF SLEEP AND RISK OF OBSTRUCTIVE SLEEP APNEA IN ADULTS WITH HIV INFECTION AT KENYATTA NATIONAL HOSPITAL (P341/06/2021)

This is to inform you that the KNH- UoN Ethics & Research Committee (KNH-UoN ERC) has reviewed and approved your above research proposal. The approval period is 16th August 2021 – 15th August 2022.

This approval is subject to compliance with the following requirements:

i. Only approved documents (informed consents, study instruments, advertising materials etc) will be used.
ii. All changes (amendments, deviations, violations etc.) are submitted for review and approval by KNH-UoN ERC before implementation.
iii. Death and life threatening problems and serious adverse events (SAEs) or unexpected adverse events whether related or unrelated to the study must be reported to the KNH-UoN ERC within 72 hours of notification.
iv. Any changes, anticipated or otherwise that may increase the risks or affect safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH- UoN ERC within 72 hours.
v. Clearance for export of biological specimens must be obtained from KNH- UoN ERC for each batch of shipment.
vi. Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. (Attach a comprehensive progress report to support the renewal)
vii. Submission of an executive summary report within 90 days upon completion of the study.

Protect to discover

Appendix 9: Similarity Report

QUALITY OF SLEEP AND RISK OF OBSTRUCTIVE SLEEP APNEA IN ADULTS WITH HIV INFECTION AT KENYATTA NATIONAL HOSPITAL

ORIGINALITY REPORT

13%	10%	12%	3%
SIMILARITY INDEX	INTERNET SOURCES	PUBLICATIONS	STUDENT PAPERS

PRIMARY SOURCES

1	Erepository.uonbi.ac.ke Internet Source	1%
2	dochero.tips Internet Source	1%
3	"Sleep Disorders Medicine", Springer Science and Business Media LLC, 2017 Publication	1%
4	www.science.gov Internet Source	1%
5	www.aidsreviews.com Internet Source	<1%
6	"Encyclopedia of AIDS", Springer Science and Business Media LLC, 2018 Publication	<1%
7	revistasaludmental.com.mx Internet Source	<1%
8	epdf.tips Internet Source	<1%