

ADDIS ABABA UNIVERSITY

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CENTER FOR FOOD SCIENCE AND NUTRITION

CARDIOMETABOLIC RISKS AMONG ADULTS LIVING WITH HIV INITIATED ON ANTIRETROVIRAL THERAPY FOLLOWING THE TEST-AND-TREAT IMPLEMENTATION IN SIDAMA REGION: DISEASE BURDEN, DETERMINANTS AND EFFECTS OF LIFESTYLE COUNSELING

By

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A Dissertation Submitted to the Center for Food Science and Nutrition of Addis Ababa University in Partial Fulfilment of the Requirements for the Degree of Doctor of Philosophy (Ph.D.) in Clinical Nutrition

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Declaration

I confirm that this PhD. dissertation is my own original work and has not been submitted to any other university for a degree. All sources of materials used in this dissertation have been properly acknowledged.

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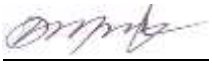
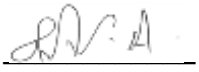
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ADIVISOR'S APPROVAL SHEET

This is to confirm that the dissertation entitled **"Cardiometabolic Risks Among Adults Living with HIV Initiated on Antiretroviral Therapy Following the Test-and-Treat Implementation in Sidama Region: Disease Burden, Determinants, and Effects of Lifestyle Counseling"** submitted in partial fulfilment of the requirements for the degree of PhD with specialization in Clinical Nutrition, the Graduate Program of the Center for Food Science and Nutrition and has been carried out **Agete Tadewos Hirigo** ID. No. GSR/0755/13, under my/our supervision. Consequently, I/we affirm that the student has met all the requirements and is hereby eligible to submit the dissertation to the Center for Food Science and Nutrition.

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CARDIOMETABOLIC RISKS AMONG ADULTS LIVING WITH HIV INITIATED ON ANTIRETROVIRAL THERAPY FOLLOWING THE TEST-AND-TREAT IMPLEMENTATION IN SIDAMA REGION: DISEASE BURDEN, DETERMINANTS AND EFFECTS OF LIFESTYLE COUNSELING

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ABSTRACT

Background: Antiretroviral therapy (ART) has significantly improved survival among people living with HIV (PLWH). With increased life expectancy, cardiometabolic risks like obesity, elevated blood pressure, hyperglycemia, dyslipidemia and metabolic syndrome (MetS) are rising in this population. Since the World Health Organization recommended test-and-treat strategy and dolutegravir (DTG) based regimens, they have been widely adopted across sub-Saharan Africa. Ethiopia implemented test-and-treat in 2017 and distribution of DTG-based regimens in 2019. However, their cardiometabolic effects in this population remain unclear.

Objective: The objective of this study was to: (1) to assess the prevalence and risk factors of high blood pressure (HBP), hyperglycemia, dyslipidemia, and metabolic syndrome (MetS); (2) evaluate trends in body weight among adults receiving first-line ART over a 24-month period; and (3) evaluate the effect of lifestyle counselling on weight and body composition among adults with overweight and obesity in Hawassa city, Sidama Region.

Methods: A mixed-methods design was employed, consisting of a retrospective cohort study (n = 524; February 2017–October 2022), a cross-sectional study (n = 465; January 5, 2023–May 30, 2024) using systematic random sampling, and a randomized controlled trial (RCT; n = 126; January 5, 2023–May 30, 2024). RCT participants were randomly assigned to intervention (n = 63) or control (n = 63) groups. Participants were selected via systematic sampling, and data were collected through semi-structured questionnaires and face-to-face interviews. Blood samples obtained from participants after an overnight fast were used to evaluate glucose and lipid profiles. High blood pressure, hyperglycemia, dyslipidemia, and metabolic syndrome (MetS) were defined

according to established guidelines. Data were entered using EPI-Data version 3.1 and analyzed with IBM SPSS version 27.0 and STATA 17.0. Statistical analyses included descriptive statistics, linear mixed-effects models, and binary logistic regression. Adjusted odds ratios (AORs) with 95% confidence intervals (CIs) were calculated, with p-values < 0.05 considered statistically significant.

Results: Over 24 months, adults initiated DTG-based regimens gained significantly more weight than those on non-nucleoside reverse transcriptase inhibitors (NNRTIs) (8.6 kg vs. 4.95 kg, $p<0.0001$), with DTG initiation associated with ≥10% weight gain (AOR=1.9; 95% CI: 1.19–3.04). HBP prevalence was 57.9%, including 40.5% prehypertension and 17.3% hypertension; 84.4% of hypertensive cases were newly diagnosed. DTG initiation (AOR=5.9; $p=0.01$) and switching to DTG (AOR=3.8; $p=0.03$) were significantly associated with HBP. Hyperglycemia prevalence was 24.4% (16.7% prediabetes, 7.7% diabetes), with 82.3% of diabetes cases newly diagnosed; age >50 (AOR=2.1; $p=0.02$), alcohol use (AOR=2.1; $p=0.04$), obesity (AOR=3.2; $p=0.01$), high waist-hip ratio (AOR=2.6; $p=0.002$), and elevated LDL-cholesterol (AOR=2.2; $p=0.04$) were significant associated with hyperglycemia. Dyslipidemia prevalence was 74.0%, most commonly low HDL-cholesterol (66.4%), and dyslipidemia associated with DTG initiation (AOR=4.8; $p=0.02$) and high waist circumference (AOR=1.06; $p=0.01$). MetS was present in 36.4% and associated with age >50 (AOR=3.2; $p=0.003$), alcohol use (AOR=2.7; $p=0.02$), body mass index ≥25 kg/m² (AOR=2.2; $p=0.03$), and high waist-height ratio (AOR=3.9; $p=0.01$). At six months, lifestyle counselling significantly reduced body weight (Δ=–1.4 kg, $p=0.002$), visceral fat (Δ=–0.53, $p=0.006$), fat mass (Δ=–2.16 kg, $p<0.001$), and body fat percentage (Δ=–2.02%, $p<0.001$), and increased skeletal muscle (Δ=+1.27%, $p<0.001$). Counselling was associated with achieving ≥3% weight loss (β=0.158, $p=0.048$).

Conclusion: The findings highlight the need to strengthen routine screening, risk stratification, and targeted lifestyle interventions within HIV care to facilitate early identification and management of the growing burden of noncommunicable diseases among PLWH on ART.

Keywords: HIV, Antiretroviral therapy, Cardiometabolic risks, Dolutegravir, Dyslipidemia, Blood pressure, Metabolic syndrome, Obesity, Lifestyle counselling, Sidama Region, Ethiopia

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Abbreviations/ Acronyms

3TC	Lamivudine
AIDS	Acquired Immunodeficiency Syndrome
AOR	Adjusted Odds Ratio
ART	Antiretroviral Therapy
AZT	Zidovudine
BFP	Body Fat Percent
BMI	Body Mass Index
ART	Antiretroviral Therapy
CI	Confidence Interval
COR	Crude Odds Ratio
CPT	Co-trimoxazole Preventive Treatment
CVD	Cardiovascular Disease
DBP	Diastolic Blood Pressure
DTG	Dolutegravir
EDTA	Ethylene Diamine Tetra Acetic Acid
EFV	Efavirenz
FAV	Fruit And Vegetable
FBG	Fasting Blood Glucose
FFM	Fat-Free Mass
FFMI	Fat-Free Mass Index
FM	Fat Mass
FMI	Fat Mass Index
FTC	Emtricitabine
HbA1c	Hemoglobin A1c
HDL-c	High-Density Lipoprotein cholesterol
HIV	Human Immunodeficiency Virus
HTN	Hypertension
INSTI	Integrase Strand Transfer Inhibitor
IPT	Isoniazid Preventive Treatment

LDL-c	Low-Density Lipoprotein cholesterol
MET	Metabolic Equivalent of Task
MetS	Metabolic Syndrome
NC	Neck Circumference
NCD	Non-communicable Disease
NCEP-ATP III	National Cholesterol Education Program Adult Treatment Panel III
NNRTI	Non-Nucleoside Reverse Transcriptase Inhibitor
N(t)RTI	Nucleoside/nucleotide Reverse Transcriptase Inhibitor
NVP	Nevirapine
PI	Protease Inhibitors
PLWH	People Living With HIV/AIDS
SBP	Systolic Blood Pressure
SPSS	Statistical Package for Social Science
SSA	Sub Saharan Africa
T2DM	Type 2 Diabetes Mellitus
TAF	Tenofovir Alafenamide
TB	Tuberculosis
TC	Total Cholesterol
TDF	Tenofovir Disoproxil Fumarate
TG	Triglyceride
VIF	Variance Inflation Factor
WC	Waist circumference
WHO	World Health Organization
WHR	Waist to Hip Ratio
WHtR	Waist to Height Ratio

Organization of the Dissertation

This dissertation is structured into six chapters:

Chapter One introduces the study, presenting the study objectives and highlighting the research gaps that this study seeks to address.

Chapter Two offers a detailed literature review on cardiometabolic risks, including clinical weight gain, blood pressure, hyperglycemia, dyslipidemia and metabolic syndrome, alongside their determinant factors. It also examines the impact of lifestyle modification counselling on body weight and composition and provides a conceptual framework for understanding the determinants of cardiometabolic risks.

Chapter Three reveals the materials and methods used in the study. It describes the study area, design, and period, as well as the source and study populations. This chapter also includes details on sample size calculation, sampling procedures, and the statistical analysis techniques applied.

Chapter Four presents the study's results, which are organized as published articles and submitted manuscripts. The sections are as follows:

- **Section 4.1** (the article published in *Annals of Medicine*, Taylor & Francis Group) describes the impact of Dolutegravir-Based first-line ART on weight and body mass index in adults living with HIV Attending Healthcare Facilities. The section covers socio-demographic characteristics, health-related factors and treatment-related factors, presented through text, tables and figures.
- **Section 4.2** (the article published in *Therapeutic Advances in Infectious Diseases*, Sage Journals Group) examines the prevalence and determinants of high blood pressure among adults with HIV on antiretroviral therapy.
- **Section 4.3** (the article published in *Endocrinology, Diabetes & Metabolism*, Wiley Journals Group) presents the prevalence and determinants of hyperglycemia among adults with HIV on antiretroviral therapy.
- **Section 4.4** (the manuscript submitted and accepted for publication in the journal of *Atherosclerosis plus*, Elsevier Journals Group) investigates the prevalence and determinants of dyslipidemia among adults with HIV on antiretroviral therapy.
- **Section 4.5** (the article published in *Therapeutic Advances in Chronic Diseases*, Sage Journals Group) examines the prevalence of metabolic syndrome and its contributing

factors in adults living with HIV who initiated first-line antiretroviral therapy after the adoption of the test-and-treat strategy.

- **Section 4.6** (the article published in *Obesity Pillars*, Elsevier Journals Group), evaluates the impact of lifestyle modification counselling on body weight and body composition among overweight/obese adults living with HIV on antiretroviral therapy through a randomized controlled trial, detailing the effects of the intervention on body weight and composition.

Chapter Five provides a comprehensive discussion of the study's findings, contextualizing the findings within existing literature and interpreting their implications.

Chapter Six concludes the dissertation by summarizing the key findings and offering recommendations based on the study results.

Chapter 1- *Introduction*

Chapter 1-Introduction

1.1. Background

Human immunodeficiency virus (HIV) is a infectious virus that weakens the immune system by targeting CD4+ T lymphocytes, which play a vital role in cell-mediated immunity.The virus binds to the CD4 surface marker, leading to excessive activation, rapid proliferation, and eventual death of these cells (Hunt et al., 2003). Since HIV suppresses the physiologic functions of immunity and destroys CD4+T cells, people living with HIV (PLWH) gradually become immunodeficient. This progressive weakening of immunity also favors the emergence of opportunistic infections as well as a variety of malignant diseases in these people (Hunt et al., 2003; WHO, 2021). Untreated PLWH may develop acquired immunodeficiency syndrome (AIDS) after several years, which is the worse-to-worst stage in which people become sensitive to various types of infections and display various clinical symptoms (Cancer.Net Editorial Board, 2019; WHO, 2021).

Since the beginning of the HIV epidemic, approximately 88.4 million (71.3–112.6 million) people have been infected with the pandemic HIV; of these, 42.3million (35.7million – 51.1 million) people have died from AIDS-related illnesses (UNAIDS, 2024). In addition, 39.9 million (36.1 million–44.6 million) are living with HIV globally and 1.3million (1.0 million–1.7 million) became newly infected in 2023 (UNAIDS, 2024). Sub-Saharan Africa (SSA) has been severely affected by the HIV epidemic, with an approximate adult infection rate of 4.2% and account for more than two-thirds of all PLWH globally (J. Unaids, 2017). Ethiopia is the second-most populous country in Africa (Worldometer, 2021) and according to the Ethiopian Public Health Institute (EPHI), had an estimated 605,238 PLWH in 2023 and 598,888 in 2024. EPHI estimates also indicated 7428 new HIV infections in 2023 and 7255 in 2024 (EPHI, 2024).

Until the mid-1990s, PLWH were expected to live for a maximum of two years after the onset of the initial AIDS-defining disease. However, in 1995, a novel form of antiretroviral therapy (ART) was introduced, significantly improving the life expectancy of PLWH. In addition, the infection has transformed from a fatal to a chronic condition, particularly in those who have been undergoing ART (Bavinton et al., 2018; Rodger et al., 2019). ART not only extends life expectancy but also significantly reduces the risk of HIV transmission by substantially suppressing viral loads in PLWH (David, Lima, Zhu, & Brauer, 2020).

Approximately 30.7 million (27 million – 31.9 million), which means 77% [61–89%] of PLWH globally were receiving highly active ART (HAART) in 2023, representing a coverage rate of 73% (UNAIDS, 2024). In addition, Ethiopia's national government has committed to achieving the global 95-95-95 targets by 2025, aiming for at least 95% of PLWH to know their status, 95% of those diagnosed to receive ART, and 95% of those on ART to achieve viral suppression. As of a 2019 report, 79% of PLWH were aware of their status, 90% of those were receiving ART, and 91% of individuals on treatment had achieved viral suppression (FHAPCO, 2021).

There are seven classes of ART drugs: nucleoside/nucleotide reverse transcriptase inhibitors or non-nucleoside reverse transcriptase inhibitors(N(t)RTIs or NNRTIs)), protease inhibitors (PIs), fusion inhibitors, chemokine receptor type 5 (CCR5) antagonists, integrase strand transfer inhibitors (INSTIs) and post-attachment inhibitors (NIH, 2021). Currently, at least three antiretroviral drugs from various classes are recommended to achieve adequate viral suppression (FMoH, 2018). These combinations involve two N(t)RTI drugs and one NNRTI or PI drug (FMoH, 2018; Piacenti, 2006).

However, the World Health Organization (WHO) now recommended dolutegravir (DTG)-based ART as the preferred treatment for PLWH in SSA (WHO, 2016). This is due to DTG's high efficacy, rapid viral suppression, low incidence of adverse events and a high genetic barrier to resistance compared with NNRTIs. Consequently, the WHO has recommended transitioning from NNRTI-based regimens to DTG-containing ART regimens. DTG combined with Tenofovir disoproxil fumarate (TDF) or Abacavir (ABC) plus lamivudine (3TC) is used as a first-line ART for people whose viral load is less than 1000 copies per mL (WHO, 2018). Moreover, in 2018, Ethiopia's Ministry of Health revised its HIV treatment guidelines to include DTG-based regimens as the preferred ART regimen for individuals aged 10 years and above and weighing ≥30kg, with the exception of pregnant women (FMoH, 2018).

1.2. Statement of the Problem

The widespread implementation of combination ART has significantly increased life expectancy among individuals living with HIV, however, cardiovascular and metabolic dysregulation are becoming serious challenges among PLWH (Lacson, Barnes, & Bahrami, 2017; Nsagha et al., 2015). PLWH on ART often experience an increased prevalence of cardiovascular disease (CVD)

risk factors including type 2 diabetes mellitus (T2DM), overweight/obesity, hypertension (HTN) and dyslipidemia (Hemkens & Bucher, 2014; Lacson et al., 2017). Despite the reduction in HIV/AIDS morbidity and mortality because of easy access to ART, SSA countries are currently confronted with a wide range of noncommunicable diseases (NCDs) (Girum, Wasie, & Worku, 2018; Semu et al., 2016). PLWH on ART may face a 26% increased risk of T2DM (Njuguna et al., 2018), a 21.5% higher risk of metabolic syndrome (MetS) (Todowede, Mianda, & Sartorius, 2019), a 70% increased risk of dyslipidemia (one of the CVD risk factors) (Calza et al., 2017) and a 26% greater likelihood of experiencing myocardial infarction (Friis-Møller et al., 2003).

In line with the WHO recommendations, older ART regimens, which had lower efficacy and higher toxicity, have been replaced with DTG-based regimens (Organization, 2020). In addition, the majority of PLWH on first-line ART have shifted to DTG-based ART in Ethiopia following the WHO approval. However, both the national and the WHO consolidated ART guidelines do not provide a clear recommendation that addressing clinical weight gain, body composition and cardiometabolic abnormalities be considered essential components of healthcare for PLWH receiving DTG-based ART regimens (FMoH, 2018; WHO, 2016). In addition to the pathophysiology of HIV, emerging studies suggest that DTG-containing ART regimens are associated with clinical weight gain and other cardiometabolic issues in SSA (Kouanfack et al., 2019; Lamorde et al., 2020).

There have been contradictory reports in previous studies, and various potential variables that may influence the cardiometabolic health of PLWH have not been evaluated in this population. For example, studies reported no significant change in body weight among PLWH on ART medications (Giacomelli et al., 2021; Guaraldi et al., 2021). Conersly, other studies have reported significant weight gain (Bourgi, Rebeiro, et al., 2020; Eckard & McComsey, 2020), including increases in both lean and fat mass, among individuals treated with DTG-based regimens compared to individuls on other regimens (Venter et al., 2019). Several studies also revealed that females who received DTG based regimens had a higher risk of weight gain (Alcorn K, 2020; Thivalapill et al., 2021), whereas another study revealed that males who received DTG based regimens were at a greater risk of weight gain (Taramasso et al., 2020). In addition, some studies have shown no association between the occurrence of diabetes and DTG based regimens ART regimens (Ursenbach et al., 2020), whereas others have reported a significant association between

hyperglycemia and DTG based treatments (Lamorde et al., 2020). Moreover, studies have revealed inconsistent findings on dyslipidemia. For instance, PLWH on DTG based regimens have an increased occurrence of lipid alteration than individuls receiving the NNRTI based regimens (Amutuhaire et al., 2023; Kigongo et al., 2024). In addition, reports indicated a higher risk of dyslipidemia-related complications in individuals received DTG-based ART (Benson M Hamooya, Patrick Musonda, et al., 2021; Jemal, Shibabaw Molla, Tiruneh G. Medhin, Chekol Abebe, & Asmamaw Dejenie, 2023; Kigongo et al., 2024) with a high incidence of low HDL-c (Benson M Hamooya, Patrick Musonda, et al., 2021) and elevated TGs (S. Liu et al., 2023). While several other studies suggest that dyslipidaemia is less prevalent or improved with DTG-based regimens compared to other regimens (Bagella et al., 2019b; Byonanebye et al., 2021; Quercia, Roberts, Martin-Carpenter, & Zala, 2015). In support, DTG has been reported as a significant treatment option for older people who may have additional risk factors for metabolic syndrome or CVD (Quercia et al., 2015).

Several studies have revealed that PLWH who received DTG based regimens are more prone to developing psychological issues such as depression and anxiety, compared to individuals on other ART regimen (Povar-Echeverría et al., 2021; Reeves et al., 2021). The associations of depression with weight gain/obesity (Provias, 2018; Sharafi et al., 2020), anxiety with abdominal fat in females (Heidari-Beni et al., 2021) and psychiatric problems with hyperlipidemia and HTN (Jia et al., 2020; Santos-Veloso et al., 2019) are well-known. Previous researches, however, have not examined the influence of psychiatric conditions on cardiometabolic problems in PLWH receiving DTG based ART by including them as independent variables.

Additionally, consuming fruits and vegetables has been linked to a reduced risk of cardiovascular diseases (Miller et al., 2017), whereas inadequate intake has been associated with an increased risk of cardiometabolic diseases (P. Verma, Srivastava, & Jain, 2018). However, the impact of FAV consumption patterns on weight, body composition and other cardiometabolic conditions has not been investigated in previous DTG based studies, despite evidence that DTG-based regimens contribute to weight gain and metabolic complications.

Thus, investigating burden and determinants of cardiometabolic risks in adult PLWH receiving ART, particularly after the adoption of the test-and-treat strategy and new ART regimens, is essential for identifying underlying factors and implementing targeted strategies to mitigate

cardiovascular risks. Additionally, assessing the impact of lifestyle interventions on weight and body composition is essential for understanding the intervention role in reducing cardiometabolic health challenges in this population.

1.3. Research objectives

1.3.1. General objective

The general objective of this study was to investigate cardiometabolic risks in adult PLWH receiving first-line regimens after the implementation of the universal test-and-treat strategy in Hawassa City, Sidama Region with a focus on disease burden, determinants and effects of lifestyle interventions, conducted from November 01, 2022 to May 30, 2024.

1.3.2. Specific objectives

- To determine the trends of weight gain and associated factors among adult PLWH on first-line ART regimens.
- To determine magnitude and associated factors of high blood pressure among adult PLWH on first-line ART regimens.
- To determine prevalence of hyperglycemia and its determinants among adult PLWH on first-line ART regimens.
- To determine prevalence and associated factors of of dyslipidemia among adult PLWH on first-line ART regimens.
- To determine the burden and associated factors of MetS among adult PLWH receiving first-line regimens.
- To assess the effects of lifestyle counseling on body weight and composition in adults with a body mass index (BMI) of ≥25 kg/m² who were receiving first-line ART regimens.

1.4. Research questions

1. What is the trend of weight after 24 months of ART initiation?
2. What are the determinants of clinical obesity among adult PLWH who are first-line regimens in Hawassa City?
3. What is the prevalence of hyperglycemia among adult PLWH receiving first-line regimens in Hawassa City adminstration?

4. What factors contribute to hyperglycemia in adult PLWH receiving first-line regimens in Hawassa City adminstration?
5. What is prevalence of dyslipidemia among adult PLWH receiving first-line regimens in Hawassa City adminstration?
6. What factors contribute to the alterations of lipid metabolism in adult PLWH receiving first-line regimens in Hawassa City adminstration?
7. What is the prevalence of elevated blood pressure among adult PLWH receiving first-line regimens in Hawassa City adminstration?
8. What are the factors associated with elevated blood pressure in adult PLWH receiving first-line regimens in Hawassa City adminstration?
9. What is the prevalence of MetS among adult PLWH receiving first-line ART regimens in Hawassa City Administration adminstration?
10. What are the determinants of metabolic syndrome in adult PLWH receiving first-line regimens in Hawassa City adminstration?
11. Does lifestyle modification counseling have an effect on weight and body composition among adults with overweight and obesity receiving first-line ART?

1.5. Significance of the study

SSA faces the dual challenge of managing the persistent HIV epidemic alongside a growing burden of NCDs, which now compete with infectious diseases for limited healthcare resources (Bigna & Noubiap, 2019; Costa et al., 2020). The successful rollout of ART has contributed to a rise in life expectancy for PLWH. However, the metabolic disorders associated with ART including cardiovascular diseases, chronic renal diseases and osteoporotic fractures, make PLWH more vulnerable to NCDs relative to the general population (Althoff et al., 2015; Rasmussen et al., 2015).

In Ethiopia, the increasing burden of both infectious diseases and NCDs poses significant health challenges, particularly for PLWH. Among the emerging health risks, cardiometabolic conditions have become a growing concern. The rising incidence of CVD among PLWH has shifted the age distribution, now affecting a younger population that was traditionally less susceptible to these conditions. This demographic shift not only increases health risks for individuals but also places additional strain on the active workforce, a vital segment of the population for the country's

economic productivity. In light of these challenges, there is a lack of data on cardiometabolic conditions among individuals who initiated ART, after the implementation of the test-and-treat strategy. Besides, there is limited data on cardiometabolic outcomes associated with DTG-based regimens in Ethiopia. Moreover, previous studies from other regions have reported inconsistent findings regarding cardiometabolic risks among individuals receiving DTG-based treatments.

Therefore, addressing the gaps in understanding cardiometabolic risks among PLWH is essential for developing targeted health policies and interventions in Ethiopia. Effectively reducing the rising cardiometabolic risks in PLWH needs assessing the burden of key conditions such obesity, dyslipidemia, hypertension, hyperglycemia, and MetS, as well as the factors that contribute to them. This approach could not only improve the health outcomes of PLWH but also help reduce the comprehensive socio-economic burden on the active workforce. Such an assessment will be also critical for developing strategies for early screening, prevention and controlling of these situations in these people. Moreover, the findings of this study could provide valuable insights for designing targeted public health policies and interventions, ultimately enhancing the effectiveness of care for PLWH and improving overall health outcomes in Ethiopia.

Chapter 2- *Literature review*

Chapter 2- Literature review

2.1. HIV Biology, pathogenesis and the Role of ART

HIV belongs to the Lentivirus genus, which belongs to the *Retroviridae* family, subfamily Orthoretrovirinae (Luciw, 1996). The virus is divided into categories 1 and 2 (HIV-1, HIV-2) based on genetic features and variations in viral antigens (Gao et al., 1999). The virus is transmitted through the exchange of certain body fluids from PLWH, including blood, breast milk, semen, and vaginal fluids, and it can also be passed from mother to child during pregnancy or childbirth (WHO, 2024). However, HIV is not spread through casual contact such as hugging, kissing, shaking hands, or sharing personal items, food, or water (WHO, 2024).

Viral ribonucleic acid (vRNA) and reverse transcriptase (RT) are responsible for the synthesis of viral DNA (vDNA), while integrase (IN) facilitates the integration of vDNA into the host genome, which are key components of the HIV-1 ribonucleoprotein (RNP) complex. The RNP is surrounded by a protective shell composed of 1600 capsid protein (CA) molecules organized in hexameric and pentameric rings (Zhao et al., 2013) that make up the viral core. The core of HIV-1 enters the cytoplasm after it fuses with the cell membrane, where it interacts with several host components, including those that aid in viral transit to the nucleus and nuclear import (Campbell & Hope, 2015; Matreyek & Engelman, 2013). Then, trimers of noncovalently connected heterodimers composed of the surface glycoprotein gp120 and the transmembrane glycoprotein gp41 make up the HIV-1 envelope spikes (J. Liu, Bartesaghi, Borgnia, Sapiro, & Subramaniam, 2008; Zanetti, Briggs, Grünewald, Sattentau, & Fuller, 2006). When these spikes are activated, they set off a chain of conformational changes that lead to the fusion of the viral and host cell membranes and the release of the viral core into the cytoplasm. CD4+ T cells and macrophages are the principal targets of HIV-1 infection (Rizzuto et al., 1998). The pathogenesis of HIV infection is driven by widespread immunological activation caused by HIV replication and the immune response to the virus. Increased T-cell turnover (production and destruction), increased T-cell death, a decrease in the size of the CD4+ T-cell pool, and activation-induced immunodeficiency are consequences of HIV-induced immunological activation (Younas, Psomas, Reynes, & Corbeau, 2016). In addition, the replication of HIV in lymph node and changes the node shape, resulting in a further decrease in CD4+ T cells (Deeks, Tracy, & Douek, 2013). A significant decrease in CD4+ cell counts, as well as increased B-cell proliferation and

hypergammaglobulinemia, are all symptoms of this AIDS. Immune activation, which has recently been re-appreciated as a primary source of the pathogenic pathway, is most likely to blame for the latter discovery (Barré-Sinoussi et al., 1983; Gallo et al., 1984).

The HIV life cycle has seven stages, each involving specific viral enzymes that enable the virus to infect CD4 cells and replicate. It begins with binding to CD4 receptors, followed by fusion with the cell membrane. Once inside, HIV uses reverse transcriptase to convert its RNA into DNA (reverse transcription). This DNA is then inserted into the host genome using integrase (integration). The virus hijacks the cell machinery to replicate HIV RNA and proteins. These components are assembled at the cell surface, and budding occurs as immature virus particles exit. Finally, protease processes these particles into mature, infectious HIV (NIH, 2025).

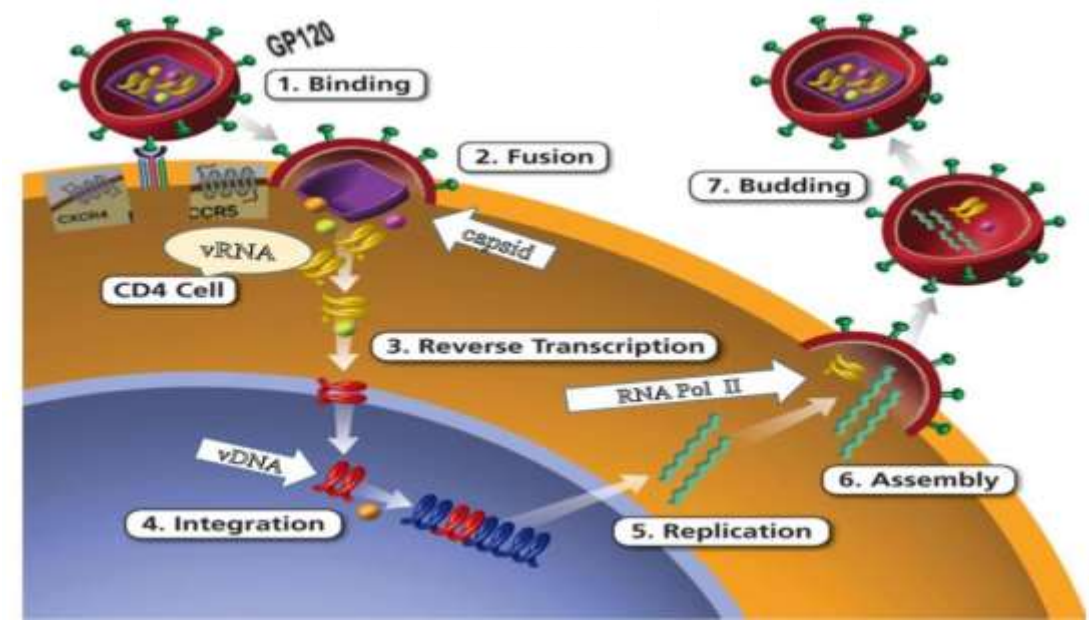


Figure 1 Understanding the HIV Life Cycle

HIV initiates infection when its gp120 envelope protein binds the CD4 receptor together with a chemokine co-receptor (CCR5 or CXCR4) on the target cell. This interaction triggers a conformational change in gp41 that fuses viral and cell membranes, releasing the viral core into the cytoplasm. Reverse transcriptase then converts the viral RNA genome into double-stranded DNA as the pre-integration complex migrates to the nucleus. There, HIV integrase permanently inserts this DNA into the host chromosome, creating a provirus. The integrated provirus is transcribed into RNA (sometimes spliced), exported to the cytoplasm, and translated into viral proteins that assemble with genomic RNA at the plasma membrane. Budding produces immature virions that undergo protease-mediated cleavage of Gag and Gag-Pol polyproteins, yielding mature, infectious particles (Chou, Maggirwar, & Marsden, 2024).

Combination ART is employed both for the prevention of HIV transmission and the treatment of HIV infection (Council, 2021). These therapies target multiple stages of the viral life cycle to effectively inhibit replication and reduce viral load. Several classes of ART drugs are currently in clinical use, each targeting distinct stages of the HIV life cycle. Pre- and post-attachment inhibitors prevent the virus from binding to host cell receptors, while fusion inhibitors block the fusion of the viral envelope with the host cell membrane, thereby preventing viral entry. Capsid inhibitors disrupt the formation and stability of the viral core. NNRTIs and N(t)RTIs interfere with the reverse transcription process by inhibiting the reverse transcriptase enzyme, preventing the conversion of viral RNA into DNA. INSTIs block the integration of viral DNA into the host genome by inhibiting the integrase enzyme, and HIV PIs inhibit the protease enzyme, thereby preventing the maturation of new viral particles (Chou et al., 2024; NIH, 2021).

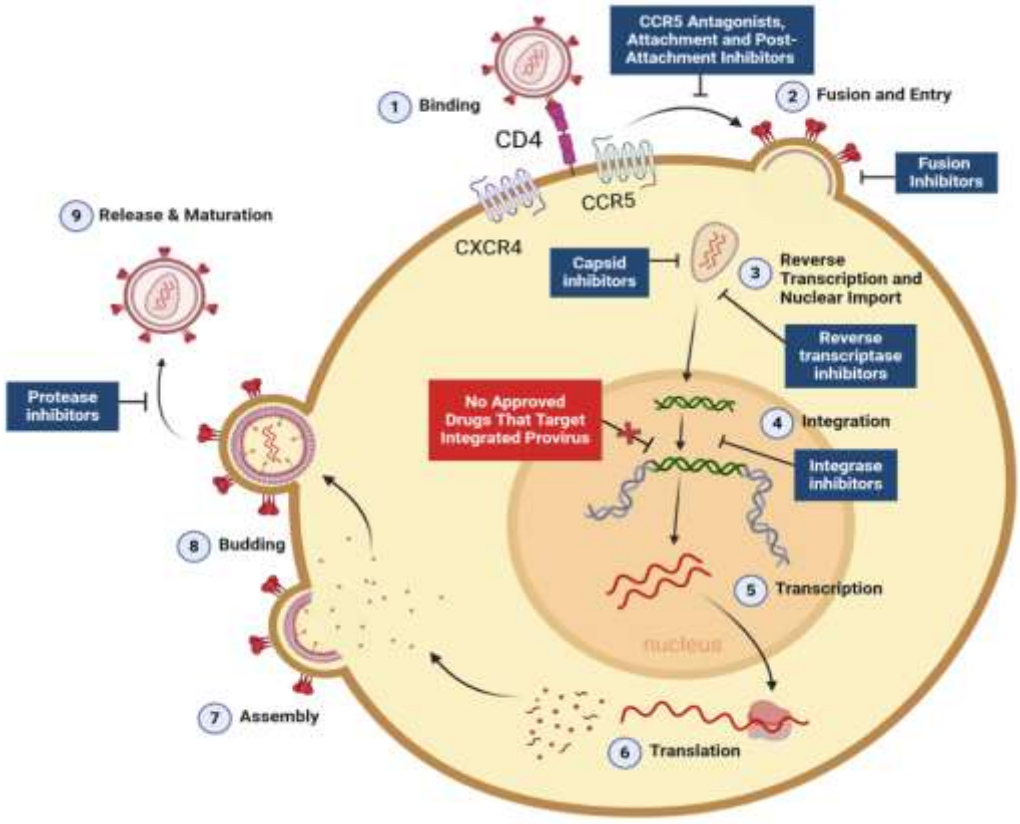


Figure 2 HIV Life Cycle Steps Targeted by Current Antiretroviral Drug Classes

Currently approved classes of antiretroviral drugs are shown in blue boxes. HIV latency occurs when the provirus pauses after integration, during which time it expresses little or no RNA and no viral proteins. As there are no currently approved antiretroviral drugs that target an integrated HIV provirus, latently infected cells can persist despite ART (red box) (Chou et al., 2024).

The introduction of combination antiretroviral medications has changed HIV from a lethal disease into a manageable chronic condition, and greatly enhancing longevity in PLWH (Lohse & Obel, 2016). However, chronic inflammation linked with prolonged HIV infection has emerged as a key factor in developing comorbidities like cancer, CVD, diabetes, obesity, hypertension and dyslipidemia (Barré-Sinoussi et al., 1983; Gallo et al., 1984). Studies have also highlighted the adverse effects of ART, particularly its association with cardiovascular risks such as diabetes mellitus, obesity, HTN, and dyslipidemia, among individuals on different ART regimens (Ekun, Fasela, Oladele, Liboro, & Raheem, 2021; Nsagha et al., 2015). This co-occurrence of HIV and CVD poses a dual health burden, reducing quality of life and leading to higher healthcare costs, including medication expenses (Girum et al., 2018; Semu et al., 2016).

2.2. HIV infection and Cardiometabolic risks

Every year, approximately 41 million people die because of NCDs, accounting for 71% of all deaths worldwide, with a disproportionate impact on people living in low-and-middle income countries (LMICs), which means approximately 31.4 million deaths each year. Of these, 15 million people die between the ages of 30 and 69 due to NCDs, accounting for 85% of premature mortality in LMICs (NCDs, 2021). In addition, each year nearly18 million people die because of CVDs and 1.5 million people die due to diabetes mellitus (NCDs, 2021).

From 2000 to 2020, new HIV infections and related deaths declined by 49% and 55%, respectively. During this period, the widespread implementation of ART saved 15.3 million lives and contributed to improved life expectancy for those PLWH (WHO, 2020b). However, more than half of PLWH have died from non-infectious comorbidities, particularly CVDs and cancers (Croxford et al., 2017; Demir et al., 2018). HIV-NCD comorbidity has emerged as a main public health concern for PLWH (Narayan et al., 2014). HIV itself contributes to a threefold greater risk of developing CVDs due to a combination of chronic inflammation and the infectious nature of the virus, compounded by the side effects of ART and the natural aging process (Narayan et al., 2014).

With improved survival rates due to increased access to ART in SSA, PLWH are now facing a growing burden of NCDs. Cardiovascular risks, in particular, are becoming more prevalent, with changes in body weight, blood pressure, lipid profile, glucose metabolism, and other key metabolic

biomarkers emerging as significant concerns for these people (Alexander Kintu, 2020; Semu et al., 2016). Moreover, HIV-NCD comorbidity has a detrimental impact on individuals receiving ART (Gonah, Moodley, & Hlongwana, 2020), impairing their health conditions. In resource limited settings, high costs for NCD treatment, which is often prolonged and expensive, quickly deplete household income. These financial strains, along with the loss of earnings, drive millions of people into poverty annually, hindering economic development. Globally, NCDs account for around 75.3% of all deaths, further exacerbating the burden on individuals and healthcare systems (Y. Wang & Wang, 2020).

2.2.1. Clinical Obesity, Altered body composition and Associated Factors

Since the introduction of ART, HIV-associated wasting and weight loss have significantly decreased, but these have been replaced by a rising incidence of weight gain (Crum-Cianflone et al., 2010). Obesity now complicates the clinical course of PLWH, increasing the risk of metabolic diseases (Bailin, Gabriel, Wanjalla, & Koethe, 2020). Abdominal and trunk lipohypertrophy have become prevalent in the ART era (de Waal, Cohen, & Maartens, 2013), with approximately 70% of PLWH on ART revealing increased abdominal fat, the most common form of fat redistribution (Dubé et al., 2007).

Cross-sectional studies conducted across Africa have revealed varying rates of obesity and overweight among PLWH on ART. In Cameroon, obesity prevalence was reported as14.5% (95% CI: 11.1-19.3) (Ngu, Choukem, Dimala, Ngu, & Monekosso, 2018) and 19.5% (Noumegni et al., 2017), while in Tanzania, it was 10% (A. Kintu et al., 2018) and 7% (Semu et al., 2016). Overweight prevalence was 28.5% in Cameroon (Noumegni et al., 2017), while it was 25% (A. Kintu et al., 2018) and 18% (Semu et al., 2016) in Tanzania. In Southeast Malawi, 17.5% of PLWH on ART were overweight or obese, and 27.8% had an increased waist-hip ratio (WHR) (Amberbir et al., 2018). A study from Cameroon further found that 40.5% of PLWH on ART had obesity defined by BMI, 33.5% had central adiposity defined by waist circumference (WC), 44.5% had central obesity determined by WHR, and 36.5% had a waist-to-height ratio (WHtR) >0.50 (Dimala, Ngu, Kadia, Tianyi, & Choukem, 2018). These findings underscore the high prevalence of obesity and visceral adiposity among PLWH on ART, which contributes to an increasing burden of cardiovascular-related health issues (Lake, 2017).

In addition, people who received NNRTI-based regimens experienced altered adipocyte function and increased inflammation, despite nevirapine's (NVP) benefits (Katlama et al., 2019). In contrast, randomized clinical trials in SSA revealed that DTG treatment led to unexpected weight gain compared to efavirenz (EFV), with increased trunk fat and a higher risk of obesity after 24 months (Bedimo, Adams-Huet, Taylor, Lake, & Luque, 2018). Moreover, initial weight gain was noted in individuals who switched from non-INSTI to INSTI-based ART regimens, as reported in observational studies (Bedimo et al., 2018; Norwood et al., 2017). In Brazil, individuals on INSTI regimens experienced significantly higher weight gain and obesity rates compared to those on NNRTI or PI regimens (Bakal et al., 2018). About 17.3% of people living with HIV (PLWH) on INSTI-based regimens gained ≥10% of their baseline weight. Among those who gained ≥10%, a higher rates were Black females (19.7%) compared to non-Black females (12.4%) (Sax et al., 2020).

The findings on body weight are inconsistent, with some studies found no significant weight changes (Guaraldi et al., 2021; Martínez-Sanz et al., 2021), while others reported substantial weight gain (Bourgi, Rebeiro, et al., 2020; Taramasso et al., 2020) including significant increases in both lean and fat mass (Venter et al., 2019) among individuals on DTG-based regimens compared to those on non-DTG regimens. A study from Cameroon reported a strong linear association of obesity with gender and ART medication use (Lake & Trevillyan, 2021). Insulin resistance is also correlated with abdominal adiposity (Lagathu et al., 2019), and concurrent increases in WC and weight gain are associated with an increase in fat mass (Lake et al., 2020). Total cholesterol (TC) and the ratio of TC/HDL-c were associated with obesity defined by the WHR (Noumegni et al., 2017). Moreover, PLWH on TAF plus emtricitabine (FTC) and DTG (TDF+FTC+DTG) regimens are at a higher risk of weight gain (Taramasso et al., 2020). Among those on DTG-based regimens who gained ≥10% of their body weight, a higher proportion were females (Sax et al., 2020), had lower baseline body weight or BMI, low baseline CD4+ cell, and/or an increased baseline HIV-1/2 RNA level (Sax et al., 2020). In contrast, other studies indicated that males on DTG regimens also experienced a higher risk of weight gain (Taramasso et al., 2020). The ADVANCE study reported an association of Tenofovir alafenamide (TAF)+FTC+DTG treatment with a substantial weight gain (≥10%) from baseline (Eckard & McComsey, 2020). Additionally, weight gain is influenced by genetic factors and gender (Lake & Trevillyan, 2021),

and anxiety also has been linked to an increased abdominal fat, particularly in women (Heidari-Beni et al., 2021).

2.2.2. Elevated blood pressure and contributing factors

HTN is a persistent elevation in blood pressure that significantly heightens the CVD risks, leading to high morbidity and mortality (Feinstein et al., 2016; Smith et al., 2014). Individuals with HIV are particularly vulnerable, experiencing CVD more frequently and at an earlier age than those without HIV, largely due to the combined effects of the viral infection and ART (Savès et al., 2003).

Global data report indicated that approximately 35% of adults PLWH have HTN, compared to 30% in the HIV-negative population (Xu, Chen, & Wang, 2017). This rate varies widely, ranging from 4% to 67%, depending on the study population, location, and time frame (Parikh et al., 2015), with an estimated prevalence of 42% among older individuals living with HIV (95% CI: 29.6–55.4) (Dakum et al., 2019). HTN was most prevalent among PLWH in North America, with a rate of 50.2% (95% CI: 29.2-71.2), followed by Europe with 37.8% (95% CI: 30.7-45.7), SSA with 31.9% (95% CI: 18.5-49.2), and Asia with 31.0% (95% CI: 26.1-36.3) (Dakum et al., 2019). Studies have consistently reported that HTN is more prevalent among individuals receiving ART compared to those who are treatment-naïve. For instance, a study conducted by Costa *et al*. from Brazil reported that 34.7% of HTN among PLWH who were receiving treatment compared to 12.7% in those who were treatment naive (Costa et al., 2020). In addition, studies across various regions reported differing HTN rates among people on ART, including 35.9% in Brazil (Costa et al., 2020) and 29% in Uganda, with 19.5% of cases classified as stage-1 HTN and 9.5% as stage-2 HTN (Lubega et al., 2021). A study conducted in Kenya found that males receiving ART had a higher prevalence of HTN (25.3%) than females (16.9%) (Mbuthia, Magutah, & McGarvey, 2021). In Ethiopia, studies have reported HTN prevalence among PLWH at 14.0% (95% CI: 10.6-17.4) (Gebrie, 2020) and 29.7% (95% CI: 25.3-35.0) (Fiseha, Belete, Dereje, & Dires, 2019).

Factors significantly contributing to HTN were age, overweight or obesity (Fiseha et al., 2019; Mbuthia et al., 2021), male sex (Fiseha et al., 2019; Mbuthia et al., 2021) and the duration of ART (Fiseha et al., 2019; Gebrie, 2020). Increased WC and WHtR were also identified as strong predictors of HTN (Adegoke et al., 2021). Additionally, factors such as a historyof alcohol use

(Mbuthia et al., 2021), educational level, monthly income, concurrent use of other medications, and central adiposity were all associated with HTN in PLWH on ART (Gebrie, 2020). Conversely, a study revealed that the duration of ART exposure is not associated with the development of HTN (Mbuthia et al., 2021). The EFV and PI-based regimens were less likely to contribute to HTN compared to NVP combined regimens (Lubega et al., 2021; Tesfay, Ziersch, Mwanri, & Javanparast, 2021). Moreover, several studies have indicated that PLWH receiving DTG-based therapy might be at a greater risk for developing psychiatric conditions such as depression (Povar-Echeverría et al., 2021; Reeves et al., 2021) and anxiety (Hsu et al., 2018; Povar-Echeverría et al., 2021). Both of these mental health issues are correlated with a higher risk of HTN (Jia et al., 2020).

2.2.3. Hyperglycemia/diabetes mellitus and associated factors

T2DM, HTN and CVDs are among the most common NCDs that coexist with HIV (Nüesch et al., 2013). While ART provides notable benefits, long-term use may lead to severe dysglycemia and impaired insulin sensitivity (Gelpi et al., 2018). Reviews from SSA indicated that T2DM and prediabetes prevalence were ranged from 11-26% and 19-47% among PLWH, respectively (Njuguna et al., 2018), while in Ethiopia, the T2DM was ranged from 6.4% to 11.4% among PLWH (Ataro, Ashenafi, Fayera, & Abdosh, 2018; Duguma & Gebisa, 2020; Gebrie et al., 2020). The rate was higher among individuals on ART medications (13.2%; 95% CI: 8-18.3) when compared to pre-ART cases (5.1%; 95% CI: 2.6-7.6) (Abebe et al., 2016). DTG-based ART regimens, on the other hand, may influence glucose metabolism (Lamorde et al., 2020). However, the mechanism underlying hyperglycemia in individuals on DTG-based regimens requires further investigation.

Studies have found an association between HIV and NCDs, which may be driven directly by the HIV infection itself or indirectly by ART medications (Hadigan & Kattakuzhy, 2014). The findings indicated the association of T2DM with central obesity and excessive alcohol intake among PLWH (Ngu et al., 2018). In addition, obesity is the primary risk factor for insulin resistance (Noumegni et al., 2017) and dysglycemia (Njuguna et al., 2018). When compared to ART navies, people who received ART medications are nearly four times more likely to develop T2DM (Dos Santos et al., 2018). Specifically, first-line regimens that contain zidovudine (AZT) were associated with a higher risk of diabetes compared to TDF-based regimens (Riyaten et al., 2015). Another studies found an association between T2DM and NNRTI regimens, older age,

ethnicity, family history and male sex (Hadigan & Kattakuzhy, 2014; Rasmussen et al., 2012). Moreover, a study reported an association between the use of DTG based regimens and the incidence of hyperglycemia (Lamorde et al., 2020). In support, the WHO database on ART medications also indicated an association between hyperglycemia and DTG based regimens at a significantly higher rate compared to other regimens (WHO, 2020a). While the other found no association between DTG and the incidence of diabetes (Ursenbach et al., 2020). Further, an association was found between a high incidence of diabetes and elevated lipid levels, particularly hypertriglyceridemia (Duguma & Gebisa, 2020; Gebrie et al., 2020).

2.2.4. Dyslipidemia and associated factors

Due to their impact on lipid profiles, several ART drugs have been linked to a greater risk of CVDs (Ryom et al., 2018). Dyslipidemia is defined by elevated levels of serum TC, TG and LDL-c, along with reduced levels of HDL-c (NCEP, 2001). Lipid derangement among PLWH is complex, involving immunological, hormonal, and genetic factors, as well as the type of ART regimen used (Fisher, Miller, & Lipshultz, 2006).

The prevalence of dyslipidemia among PLWH on ART varied according to the treatment regimen, individual lifestyle, genetic predisposition, treatment duration and other factors. According to studies, the prevalence of dyslipidemia was 10.8% in Saudi Arabia (Farahat et al., 2020), and 67.3% in Thailand with the most frequently occurring dyslipidemia of low HDL-c (46.9%) and high TGs (27.4%) (Aurpibul, Namwongprom, Sudjaritruk, & Ounjaijean, 2020), 47% in Kenya (Tilahun et al., 2021), 70.2% in Cameroon (Bekolo, Nguena, Ewane, Bekoule, & Kollo, 2014) and 74.7% in Peru (Rondan et al., 2017). An inconsistent prevalence of dyslipidemia has been reported among people on ART in Ethiopia, with a rate of 74.8% in Addis Ababa (Kemal, Teshome, & Ahmed, 2020), 77.8% in Addis Ababa (Yazie, 2020), 82.3% in Hawassa (Tadewos, Addis, Ambachew, & Banerjee, 2012), 59.9% in North-Shewa (Fiseha, Alemu, Dereje, Tamir, & Gebreweld, 2021). Hypercholesterolemia was found in approximately 29% of ART individuals in Ghana (Appiah, Sarfo, Huffman, Nguah, & Stiles, 2019), while 15.5% in Malawi (Amberbir et al., 2018), while 15.5% in Malawi (Amberbir et al., 2018), and 29.8% in Cameroon (Bekolo et al., 2014). In Ethiopia, however, the rate was greater, with 43.4% in Hawassa (Tadewos et al., 2012), 42.9% in Addis Ababa (Yazie, 2020), and 47.3% in North Shewa (Fiseha et al., 2021). Moreover, the prevalence of dyslipidemia was reported as 30.9% for TG, 19.4% for HDL-c, and 29.6% for

LDL-c (Fiseha et al., 2021). In another study, the corresponding rates were 55.5%, 43.4% and 33.6%, respectively (Tadewos et al., 2012), 31.7%, 41.3% and 22.2% (Yazie, 2020), and 51.8%, 18.4% and 33.3% (Bekolo et al., 2014), respectively. Conversely, several other studies have reported lower rates of dyslipidemia in individuals DTG-based combinations, suggesting its potential as a treatment option for older adults with comorbid health risks (Martínez-Sanz et al., 2021; Quercia et al., 2015).

Combinations of certain NRTIs with EFV have been associated with dyslipidemia, but PI-based regimens are more likely to cause significant disruptions in lipid metabolism (Molla Abebe et al., 2014). On the contrary, a Chinese research found that PLWH receiving TDF+3TC+EFV had a lesser rate of dyslipidemia than those on other first-line ART regimens (L. Q. Sun et al., 2020). Despite contradictory results, studies have demonstrated that the length of HIV infection, the type of ART regimen utilized and the extent of immunosuppression are all associated with an elevated risk of dyslipidemia (Kazooba et al., 2017). In addition, older age (Rondan et al., 2017) and BMI were significantly associated with dyslipidemia in those who were receiving ART medications (Rondan et al., 2017). PLWH who switched to DTG combined regimens, particularly those who previously received boosted PI-based regimens (Bagella et al., 2019a) had a lower lipid profile and DTG indicated as a safer drug regarding dyslipidemia (Quercia et al., 2015). Moreover, a report indicated that depression and anxiety have been associated with hyperlipidemia (Jia et al., 2020). To be clear, the situation has not been adequately explored to conclude DTG and its overall influence on lipid profile.

2.2.5. Metabolic syndrome and associated factors

Central obesity, high blood sugar, lipid alterations and elevated blood pressure are all indicators of cardiometabolic risk, commonly referred to as MetS (Husain et al., 2017; Nguyen, Peer, Mills, & Kengne, 2016). Morbidity and mortality from CVDs are more common in those people with MetS (Alberti et al., 2009). The pathogenesis of MetS is complex and multifactorial, and it may be related to aging, HIV and inflammatory conditions, the side effects of ART medications, and the activation of immune system (Non, Escota, & Powderly, 2017).

Several cross-sectional studies conducted in different regions have found varying rates of MetS among PLWH, such as 10.6% in Thailand (Aurpibul et al., 2020), 34% in the United States (Sears

et al., 2019), 40.1% in India (Sneha Deepak Mallya, Reddy T, Kamath, Pandey, & Saravu, 2020), 19.2% in Kenya (Kiama et al., 2018), 22% in Poland (Rogalska-Płońska, Grzeszczuk, Rogalski, Łucejko, & Flisiak, 2018), 20.9% in (Calza et al., 2017) and 27% in the Democratic Republic of the Congo (Katoto et al., 2018). In addition, systematic review of cross-sectional studies revealed the prevalence of MetS as 34.89% (95% CI: 26.77–43.01) by NCEP criteria and 27.92% (95% CI: 21.32–34.51) using IDF criteria among people receiving ART. Moreover, the rate was higher in females (36.74% by IDF and 34.09% by NCEP) compared to males (22.22% by IDF and 24.82% by NCEP) (Ambachew et al., 2020).

HIV infection itself (Calza et al., 2017), low baseline CD4+ cell count (Rogalska-Płońska et al., 2018), overweight or obesity (Calza et al., 2017; Vargas-Pacherrez et al., 2020), female sex (Vargas-Pacherrez et al., 2020), aging (Vargas-Pacherrez et al., 2020), taking PI-based regimens and duration since ART experience (Calza et al., 2017) were all found to be strongly associated with high-risk factors of MetS. Sedentary behavior (Macías et al., 2021) and a family history of HTN (Vargas-Pacherrez et al., 2020) were also associated MetS and its components.

ADVANCE trial study conducted in South Africa revealed that people treated with TAF+ FTC + DTG had a higher risk of MetS and obesity than those who received other ART regimens (Alcorn, 2019). In contrast, a single dose of an INSTI had a reduced risk of developing MetS (Calza et al., 2017). Additional investigations are needed to clarify the relationship between MetS and DTG-based regimens and the effect of MetS on ART outcomes in this population (B. M. Hamooya et al., 2021).

2.3. Effects of lifestyle interventions

According to the reports of recent studies, various ART regimens has been associated with weight gain in varied levels (Bourgi, Rebeiro, et al., 2020; Venter et al., 2019). However, modest weight losses could provide significant long-term health benefits for adults with obesity in the general population (Members et al., 2014; Swift, Houmard, Slentz, & Kraus, 2018). In addition, behavioral interventions that focused on dietary intake as well as and physical exercise can be considered as the first-line strategy for individuals who seeking to lose weight and tackle the effects of obesity (Heymsfield & Wadden, 2017; Jensen et al., 2014). In support, a weight loss of at least 3% from baseline can improve clinically significant cardiometabolic risks (Ahmad Zamri et al., 2020;

Jensen et al., 2014). This reduction in weight enhances insulin sensitivity and leads to better outcomes in both traditional (TGs) and non-traditional (non-HDL-c and HDL/LDL particle size) cardiovascular risk factors (Swift et al., 2018). Dietary interventions (Curry et al., 2018; Durrer Schutz et al., 2019), such as modifying eating habits, implementing caloric restriction (reducing energy intake by at least 500 kcal/day), and limiting carbohydrate intake can support weight loss and metabolic risks among overweight or obese individuals (J. Sun et al., 2023). In addition, evidence indicates early interventions on dietary intake and physical exercise can significantly improve health outcomes and reduce HIV and its treatments adverse effects on cardiometabolic health and psychological well-being (Botros, Somarriba, Neri, & Miller, 2012). Nutritional counselling coupled with aerobic exercise resulted in notable enhancements in cardiovascular fitness, body composition, and overall quality of life among PLWH (John et al., 2018).

2.4. Summary of the Literature Review: what is known and what are the gaps?

With improved survival rate due to an increased access to ART in SSA, PLWH are now facing a growing burden of NCDs. Cardiovascular risks, in particular make up a significant proportion of these conditions are clinical obesity, increased blood pressure, lipid alterations, dysglycemia and others (Girum et al., 2018; A. Kintu et al., 2018; Semu et al., 2016). Due to their efficacy, DTG based regimens are widely adopted in SSA, including Ethiopia (WHO, 2019). However, studies on cardiometabolic risks following the initiation of, or switch to, these regimens remain limited. Existing observational and clinical trial data yield inconsistent findings regarding their impact on metabolic and cardiovascular health, as outlined below.

1. Previous studies showed inconsistent results regarding body weight changes in relation to DTG-based regimens. Some reported insignificant changes (Guaraldi et al., 2021; Hickey et al., 2023), while others indicated substantial weight gain, including increases in both lean and fat mass (Bourgi, Rebeiro, et al., 2020; Martínez-Sanz et al., 2021; Sax et al., 2020; Taramasso et al., 2020). Additionally, gender-specific differences were observed, with some studies suggesting a higher risk of weight gain in females (Lake et al., 2020; Thivalapill et al., 2021), while others reported a greater risk in males (Taramasso et al., 2020). These inconsistencies highlight the need for further investigations to clarify the variations and the underlying factors.

2. Controversial reports have emerged regarding the association between DTG-based regimens and cardiometabolic risks, including hyperglycemia. A study revealed that people who started or switched to DTG-based treatments had a higher risk of developing hyperglycemia (Lamorde et al., 2020), while other reported no correlation between DTG based regimens and these conditions (Ursenbach et al., 2020). In order to realise the relationship between DTG-based regimens and cardiovascular outcomes, further investigations is required.

3. Additionally, reports indicated inconsistent findings concerning the impact DTG-based regimens on lipid metabolism. Some reported a higher incidence of dyslipidemia and related complications (Amutuhaire et al., 2023; Kigongo et al., 2024) such as low HDL-c (Benson M Hamooya, Patrick Musonda, et al., 2021; Musekwa, Hamooya, Koethe, Nzala, & Masenga, 2021) and elevated TGs (S. Liu et al., 2023) among people who received DTG-based regimens compared to those treated with other regimens (Amutuhaire et al., 2023; Kigongo et al., 2024). However, several other studies reported less frequent or improved dyslipidemia with the use DTG-based regimens (Bagella et al., 2019a; Byonanebye et al., 2021; Quercia et al., 2015). These discrepancies also highlighted the need for further studies to explain the impact of DTG on lipid profiles and related health outcomes.

4. Most of the previous studies conducted on cardiovascular risks were among individuals who initiated their ART based on low CD4+ count and or advanced clinical stage. However, this study aimed to explore metabolic and cardiovascular risks following adoption of the WHO test-and-treat strategy (HIV, 2016), which focuses treatment initiation based solely on HIV positive result, irrespective of CD4+ cells or the WHO clinical staging. This shift in treatment approach may have led to different metabolic and cardiovascular risks outcomes, emphasizing the need for further investigation to better understand its impact.

5. Ethiopia has implemented integrated HIV and NCDs care in ART clinics, but lifestyle interventions like counselling on dietary habit, energy restriction and physical activity promotion are not consistently offered to overweight and obese people on ART. The increasing obesity, partly due to newer ART medications coupled with sedentary behaviors highlight the importance of controlled studies to assess the impact of these interventions and to address their evidence-based relevance.

Therefore, the purpose of this study was to assess the burden of cardiometabolic risks in Ethiopia among adults who began ART following the adoption of universal test-and-treat, with particular focus on the impact of DTG-based regimens. Despite emerging evidence, the impact of these regimens on cardiometabolic health remained underexplored in SSA (Benson M Hamooya, Lloyd B Mulenga, et al., 2021a), especially in Ethiopia. Therefore, this study aimed to assess clinical weight gain, high blood pressure, hyperglycemia, dyslipidemia and MetS among adults on ART in in Sidama Region. Additionally, it aimed to investigate the impact of lifestyle modifications counselling on weight and body composition in overweight and obese individuals on first-line ART.

2.5. Conceptual framework

This proposed conceptual framework was developed through a review of previously published literature that highlights the complex interplay among HIV-related factors, biological and behavioral determinants, ART medications, and socio-environmental influences on the cardiometabolic health of PLWH. A comprehensive understanding of these risk factors is essential for designing targeted strategies to reduce the burden of cardiometabolic diseases in this population (figure 3).

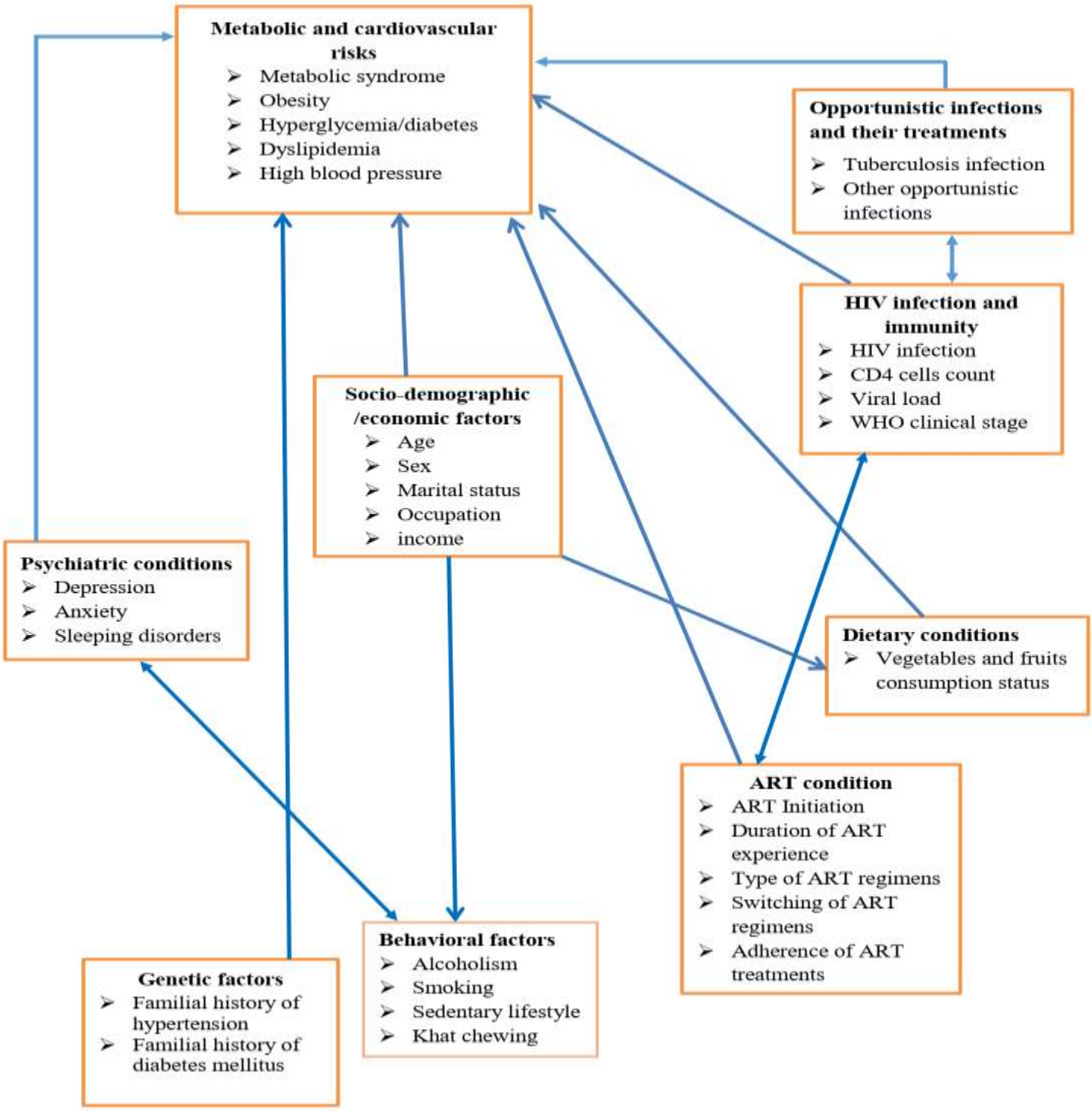


Figure 3 Conceptual framework for cardiometabolic risks in adults with HIV on antiretroviral therapy: a review of the Literature

Abbreviations: *ART, antiretroviral therapy; HIV, human immunodeficiency syndrome; WHO, World Health Organization*

Chapter 3- *Methods and Materials*

Chapter 3- Materials and Methods

This dissertation included three major parts. The first part examined trends of weight among individuals who initiated on first-line ART following the adoption of the test-and-treat strategy in Sidama Region, using a retrospective cohort study design. The second part consisted of cross-sectional studies that assessed the prevalence of elevated blood pressure, hyperglycemia, dyslipidemia, and metabolic syndrome in this population. The third presented an interventional study that employed a randomized controlled trial to evaluate the effects of lifestyle counselling on weight and body composition among adults with a BMI of ≥25 kg/m².

3.1. Overview of the Study Area

We conducted this study in Hawassa City administration in Sidama region, located approximately 275 kilometers south of Addis Ababa, the capital of Ethiopia. The city administration spans an area of 157.2 km^2, and is divided into 8 sub-cities and 32 kebeles (figure 4). The 2022 population estimate from the City Health Department indicated 402,903 people, with 201,371 females and 201,532 males. Currently, over 80 healthcare facilities are serving the population of the city, including 5 public hospitals, 8 private hospitals, 1 military hospital, 11 public health centers, 17 health posts and more than 50 private clinics. ART is being provided to PLWH in the city in three public and one private hospitals, two public health centers and two non-governmental health institutions. The health facilities include Adare General Hospital, Alatyon Hospital, Hawassa University Comprehensive Specialized Hospital, Hawela-Tulla General Hospital, Bushulo Health Center, the Family Guidance Association of Ethiopia (Hawassa branch), Millennium Health Center and Tulla Health Center.

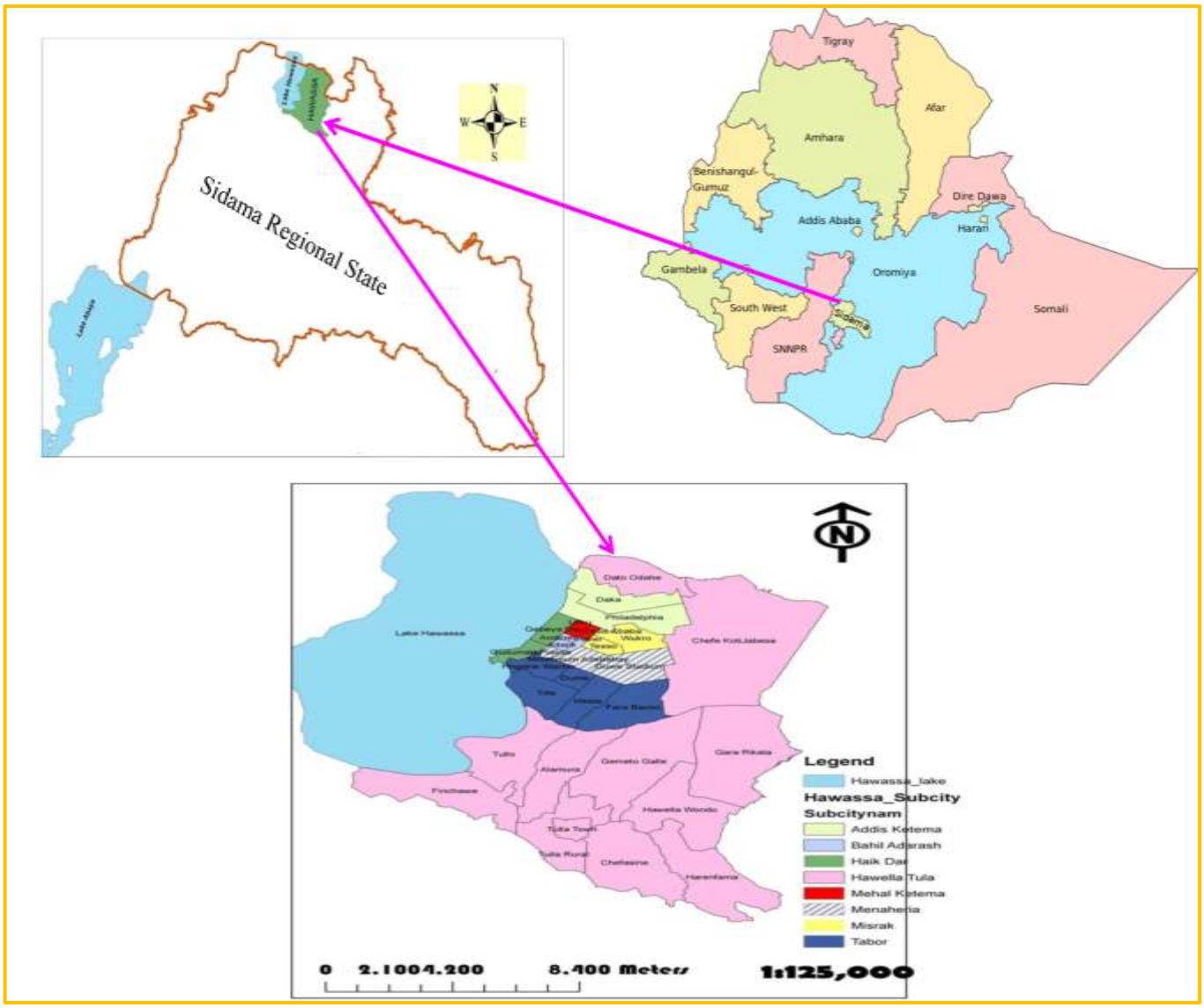


Figure 4 Map of the Hawassa city administration (study area) in Sidama region, Ethiopia

3.2. Population

3.2.1. Source population

PLWH receiving ART and follow-up care at healthcare facilities within the Hawassa City Administration, Sidama Region, were the source population for all objectives of this study. During the study period, over 6,300 PLWH were actively receiving ART and follow-up care at healthcare facilities in the City Administration. However, because of their private decisions, individuals from two health care facilities were excluded from participating in the study.

3.3. Description of Methods for Evaluation of Clinical Weight Gain

3.3.1. Study design and time frame

This study involved a retrospective cohort study design based on the medical records of adult PLWH who were undergoing first-line ART from February 20, 2017, to October 2022. The review of these medical records took place from November 1 to December 15, 2022.

3.3.2. Study population

Adult PLWH, aged at least 18 years, who were on first-line antiretrovirals and follow-up care at healthcare facilities within the Hawassa City Administration were the study population.

3.3.3. Sampling size determination

The study was conducted at seven health institutions within the Hawassa City Administration that provide ART services such as Adare General Hospital, Hawassa University Comprehensive Specialized Hospital (HUCSH), Hawella Tula General Hospital, Tula Health Center, Alatyon Hospital, Millennium Health Center and Bushulo Health Center. This retrospective study involved reviewing the medical records of adult PLWH who started ART between February 20, 2017, and October 30, 2022, and had been receiving first-line ART for a minimum of 24 months at the selected health facilities. Each medical record underwent a thorough screening process to determine eligibility based on pre-established inclusion and exclusion criteria.

3.3.4. Inclusion and exclusion criteria

3.3.4.1. Inclusion criteria

All people with HIV who were 18 years or older, have been on first-line regimens for no less than two years and commenced treatment after the launch of the universal test-and-treat initiative in Ethiopia (February 2017) (FMoH, 2017) were included in the study. We only included adult PLWH with HIVribonucic acid (HIV-RNA) <1000 copies/mL after 12 months of ART initiation. For analysis of weight and BMI, the following ART regimen groups were included: (1) Those who were treated with two (N(t)RTIs) plus DTG for a period of 24 months, and who had at least five consecutive weight measurements starting from the baseline (DTG-based arm). (2) Individuals who received two N(t)RTIs plus one NNRTI at baseline and later switched to a DTG-based

regimen within 24 months were included if they had been on the initial NNRTI-based regimen for a minimum of six months before switching and/or had at least one weight measurement after switching during the 24-month follow-up (switched arm). (3) Individuals in the comparison group initiated treatment with two N(t)RTIs plus one NNRTI at the baseline, adhered to the same treatment plan for the entire 24 months follow-up, and had a minimum of five weight measurements from the baseline during this period (NNRTI-based arm).

3.3.4.2. Exclusion criteria

People who had low adherence to ART(missing 6 or more doses from a 30-dose or over 9 doses from a 60-dose as per the guidelines) were excluded (FMoH, 2018). Participants who transferred from other health facilities, switched to DTG-based regimens before completing six months of their initial treatment, or were pregnant at any time during the 24 months follow-up were not part of the study. In addition, individuals without baseline and follow-up weight data for a minimum of 24 months, as well as those lost to follow-up before completing 24 months were excluded from the analysis.

As a result, 524 records of adults on first-line ART regimens were analyzed from ART clinics across the study's health facilities (Figure 5).

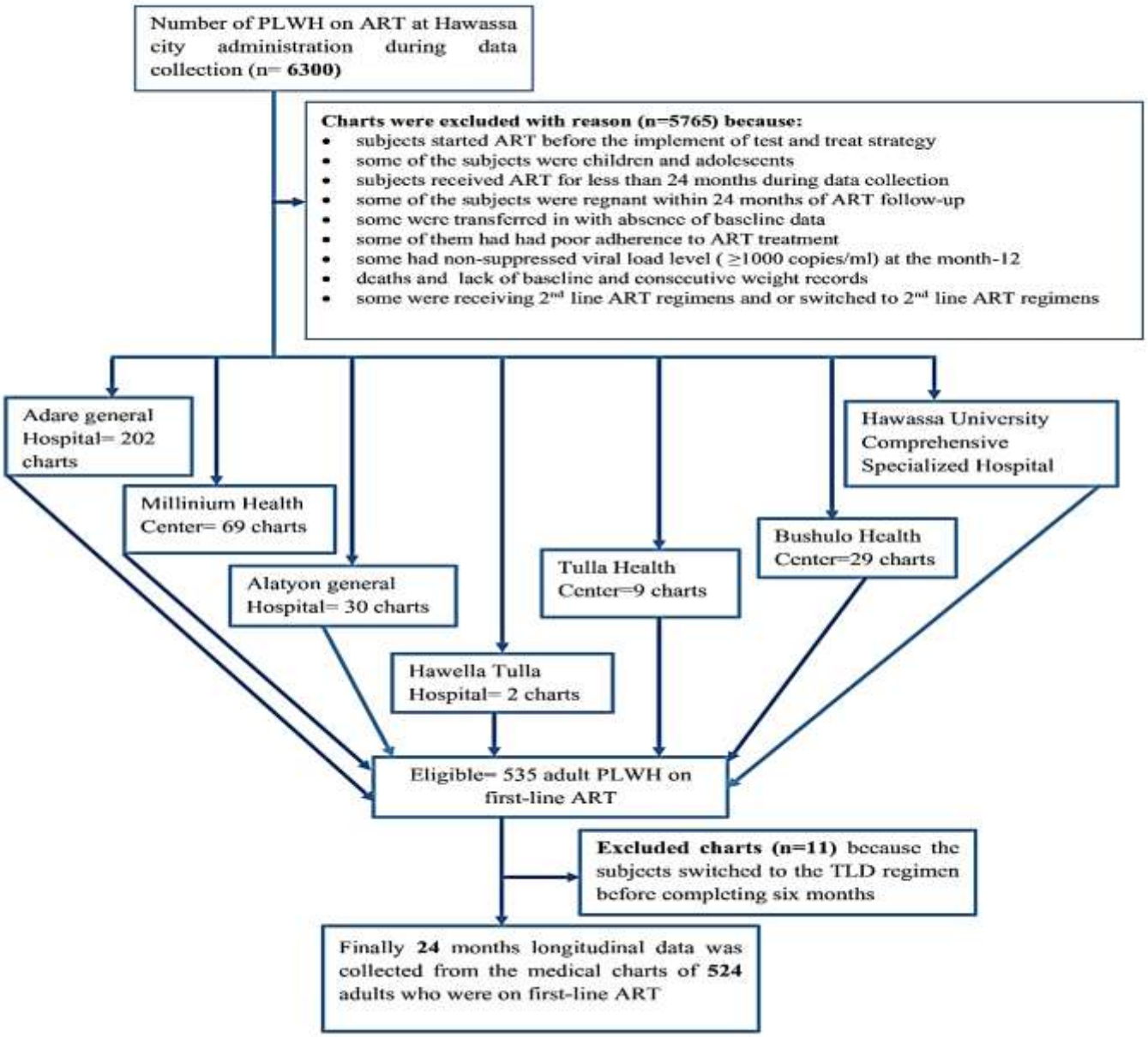


Figure 5 Flow chart indicating the study subjects' enrolment procedure at Hawassa city administration, Sidama region

Abbreviations: *ART, antiretroviral therapy; TLD, Tenofovir disoproxil fumarate plus lamivudine and dolutegravir; PLWH, people living with HIV*

3.3.5. Study variables

3.3.5.1. Outcomes

The outcome (dependent) variables were body weight and BMI. Weight gain from baseline was calculated for each individual by determining absolute change and the percentage change using the formula: [(Weight at x-month − Weight at baseline) / Weight at baseline] × 100 (Van Leth et al., 2004). Moderate weight gain was defined as a 5% to <10% increase, while excess weight gain was considered as either a ≥10% increase in weight or a BMI increase of ≥1 kg/m² after 12 or 24 months of treatment (Bourgi, Rebeiro, et al., 2020; Eckard & McComsey, 2020; Pérez, Chow, Kania, Goldberg, & Badowski, 2020; Sax et al., 2020; Taramasso et al., 2020). For individuals with recorded height, BMI was calculated using the formula: BMI = Weight (kg) / Height (m)² and categorized as underweight (<18.5 kg/m²), normal weight (18.5–24.9 kg/m²), overweight (25.0–29.9 kg/m²), or obese (≥30 kg/m²) (Garrow & Webster, 1985).

3.3.5.2. Independent variables

Socioeconomic and clinical factors were the explanatory variables in this study. Socio-demographic characteristics included age, sex, and marital status, place of residence, occupation, and education level. Clinical factors included tuberculosis (TB) co-infection and treatment, functional status (working, ambulatory, or bedridden), WHO clinical stage (I–IV), and baseline ART regimens. Baseline regimens included TDF, AZT, or ABC combined with 3TC and either NVP or EFV, or TDF or ABC combined with 3TC and DTG. Additional clinical variables included TPT, CPT, comorbid conditions (e.g., DM, cancer, HTN), and ART regimen modifications (e.g., switching from NNRTI-based to other NNRTI-based or DTG-based first-line regimens).

3.3.6. Checklist and Data collection

A checklist derived from the treatment initiation and monitoring forms used in ART clinics was employed to collect data from each participant's medical records. Prior to data collection, the alignment between the checklist and the recording system was verified by reviewing a randomly selected sample of ART case charts, and adjustments were made as needed. Achecklists included the following information: socio-demographic factors, clinical information, HIV infection and its treatment information, weight values over a 24-month period and height values for each individual. All required information of the study participants was gathered from their medical records by

trained health professionals (nurses) at the respective health facilities under the strict observation of the principal investigator.

3.3.7. Data Processing and Statistical Analysis

Continuous variables were summarized using means with 95% confidence intervals (CIs) or medians with interquartile ranges (IQRs). Depending on the data type, baseline demographic and clinical characteristics were compared across treatment groups using Pearson's χ^2 test, independent t-test, or one-way ANOVA. Our target was to evaluate the interaction between time and DTG on BMI and weight (W) adjusting for age, sex and TB co-infection. A linear mixed-effects model with an autoregressive error structure of order 1 (AR1) was constructed to analyze changes in BMI and W (ΔBMI/W = BMI/W_exam − BMI/W_base) over time. The model included time, DTG use, age, sex, TB co-infection at baseline, and the time interval (Δtime) as fixed effects. The general model structure was ΔBMI/W = β*time* + *β*DTG + β*other covariates + intercept (where β represents the regression coefficient for each variable). Each individual was treated as a random effect to account for individual variability. The interaction term between time and DTG was specifically assessed to evaluate its effect on changes in BMI and weight.The primary outcome of interest was a ≥10% weight gain over two years of treatment. DTG-based first-line regimens on ≥10% weight gain was further examined by multivariable logistic regression model, adjusting for covariates. Multicollinearity within independent factors was assessed by the variance inflation factor (VIF) before multivariable analysis, with a VIF <10 considered acceptable. Then all covariates with a p value <0.25 in bivariable analysis were included in the multivariable model except for sex. The model's goodness of fit was tested using the Hosmer and Lemeshow test and a p value >0.05 indicating good fit. A p-value <0.05 was established for statistical significance. The linear mixed-effects analysis was performed using STATA version 17.0, while data entry and other statistical analyses were done using IBM SPSS 26.0.

3.4. Description of Methods for Evaluating Blood pressure, Blood glucose, Lipid profiles and metabolic syndrome

3.4.1. Study Design and Study period

Cross-sectional studies were conducted in health facilities in Hawassa city between January 5, 2023, and May 30, 2024 as indicated in the Table 1.

Table 1 Study title of the cross-sectional studies conducted on adults with HIV on first-line antiretroviral treatment from January 05, 2023– May 30, 2024

Manuscript	Study Title	Study design	Population details	Study period
01	The association between dolutegravir based antiretrovirals and high blood pressure among adult PLWH in Sidama Region	Cross-sectional	Adult PLWH	January 05, 2023– May 30, 2024
02	Prevalence of hyperglycemia and associated factors in adult PLWH receiving first-line regimens in Sidama Region	Cross-sectional	Adult PLWH	January 05, 2023– May 30, 2024
03	The association between dolutegravir-based regimens and altered lipid metabolism among adult PLWH in Sidama Region	Cross-sectional	Adult PLWH	January 05, 2023– May 30, 2024
04	Prevalence of MetS and associated factors among Adult PLWH on First-Line regimens in Sidama Region	Cross-sectional	Adult PLWH	January 05, 2023– May 30, 2024

3.4.2. Study population

Adults aged 18 to 65 years living with HIV who were on first-line treatment regimens and had a follow-up care at healthcare facilities within the Hawassa City Administration were the study population.

3.4.3. Sampling size and sampling technique

The sample size estimation was done using Epi Info Version 7.0 software, considering a single population proportion formula. To estimate the sample size for this study, a 95%CI and a margin of error (d) of 0.05% were considered. The prevalence rates from previous studies in PLWH on ART were used to estimate the sample size for outcome variables such as 16.04% for diabetes

(Belay et al., 2021), 15% for prediabetes (Fiseha & Belete, 2019), 23.9% for MetS (Moyo-Chilufya et al., 2023) and 18.5% for HTN (Badacho & Mahomed, 2023).

$$\mathbf{n = [(Z_{\alpha/2})^2 * p*(1-p)/d^2] \times DEFF}$$

where: n = required sample size; $Z\alpha/_2$ =1.96 (95%CI); p = proportion of dependent variables; d = margin of error=0.05); DEFF = design effect: [DEFF = 1 + δ(n-1), where δ, intraclass correlation coefficient=0.0647]= (1+(8-1)x 0.0647) (Barnhart et al., 2016) = 1.5.

In addition, the factors associated with each outcome variables were also used to calculate and address the maximum representative sample size: assuming a proportion of HTN, dyslipidemia, MetS, and diabetes among PLWH who were not exposed to risk factors, exposed to unexposed ratio of 1:1, a power of 80%, odds ratios and 95% CI. The first calculated maximum sample size was 279, based on a 23.9% prevalence rate of MetS (Moyo-Chilufya et al., 2023) (Table 2). After considering a 10% non-response rate and a DEFF of 1.5, the final sample size required for representation was found to be 465. Data for the study was collected from six health facilities that provide ART services in the Hawassa city area. A sample size of 465 was allocated proportionally, based on the number of PLWH on first-line regimens at each facility. The sampling intervals (K^{th}-value) were calculated by dividing the number of PLWH on first-line treatments by the sample size assigned to each health center (N/n) (figure 6). After that, a systematic random sampling method was used to choose participants from each facility. If the participant selected by the sampling procedure met the exclusion criteria, then the next individual was included in the study.

Table 2 Determination of Representative Sample Size for Blood Pressure, Hyperglycemia, Dyslipidemia and Metabolic Syndrome Based on Study Objectives.

No	**Variables in PLWH**	**Prevalence rate**	**Sample size**	Reference
1.	HTN among PLWH on ART in Zambia	18.4%	231	(Musekwa et al., 2021)
2.	MetS among PLWH on ART in SSA	23.9%	279	(Moyo-Chilufya et al., 2023)
3.	Dyslipidemia among PLWH on ART in Ethiopia	15.1%	197	(M. Abebe et al., 2014)
4.	Diabetes among PLWH on ART in Ethiopia	16.0%	206	(Belay et al., 2021)
5.	Prediabetes among PLWH on ART in Ethiopia	15%	196	(Fiseha & Belete, 2019)
6.	HTN among PLWH on ART in Ethiopia	18.5%	232	(Badacho & Mahomed, 2023)
7.	Dyslipidemia among PLWH on ART in Eritrea	86.6%	178	(Achila et al., 2022)
	Factors associated with the study objectives			

No	**Exposure**	**rate in ART exposed**	**rate in ART unexposed**	**Odds ratio**	**Ratio (Exposed vs. unexposed)**	**Sample size**	References
1.	DTG vs. NNRTI (for HTN)	46.9%	39.1%	2.4	1:1	186	(Musekwa et al., 2021)
2.	ART vs. pre-ART (for MetS)	25%	22.5%	3.8	1:1	94	(Tesfaye et al., 2014)
3.	Insulin resistance for MetS	31.7%	9.8%	2.74	1:1	278	(Shidhaye, Ghate, Gurav, Gupte, & Panda, 2023)
4.	ART vs. pre-ART (for dyslipidemia)	23%	7.1%	3.89	1:1	184	(M. Abebe et al., 2014)
5.	ART vs. pre-ART (for new onset of DM)	52.5	45.7	12	1:1	40	(Sarfo et al., 2021)

Sample size was calculated at 95%CI , 80% power, and a 5% alpha error

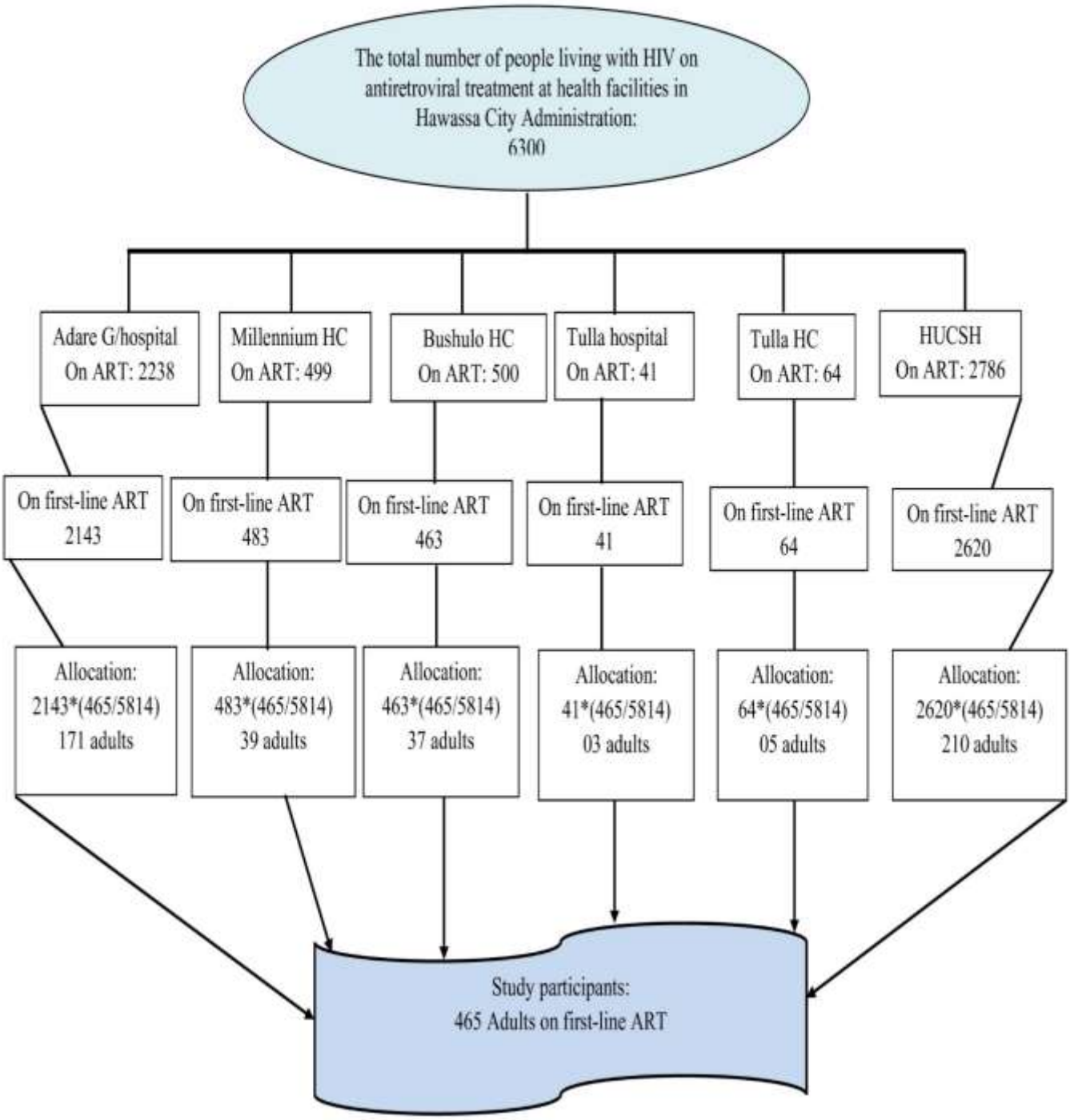


Figure 6 Schematic presentation of the sampling procedure for cross-sectional studies

3.4.4. Inclusion and exclusion criteria

3.4.4.1. Inclusion criteria

All PLWH aged 18 to 65 years, who initiated first-line ART after the adoption of test-and-treat in Ethiopia in February 2017 (FMoH, 2017; WHO, 2015) were considered for inclusion in the study. In addition, participants were required to have been on first-line ART for at least 12 months and to have achieved viral suppression (HIV-RNA <1,000 copies/mL) at 12 months of therapy to be included in the study. The inclusion criteria also encompassed individuals who initiated and remained on first-line DTG-based regimens, those who switched from NNRTI-based to DTG-based first-line regimens, and those who initiated and remained on NNRTI-based first-line ART regimens.

3.4.4.2. Exclusion criteria

The study excluded the following individuals: (1) those on ART with communication barriers, such as severe hearing impairments or deafness, to ensure reliable data collection; (2) individuals on lipid-altering medications, as documented in their medical records; (3) pregnant or lactating women; (4) individuals with documented psychiatric disorders or those receiving antipsychotic treatment prior to ART initiation; (5) individuals with physical disabilities that could affect accurate anthropometric and body composition assessments; and (6) those with confirmed liver or renal impairments.

3.4.5. Study variables

3.4.5.1. Outcome (dependent) variables

The outcome variables were blood pressure (systolic and diastolic), fasting blood glucose (FBG) concentration, lipid profile (TC, HDL-c, LDL-c and TGs level) and MetS.

3.4.5.1.1. Blood pressure and its assessment

Before measuring their blood pressure, participants were advised to rest comfortably for 10 minutes. During this time, participants sat in a quiet, private data collection room, uncrossing their legs and ankles. Then, a digital blood pressure monitor (Heuer, model 16-200) was used to measure systolic blood pressure (SBP), diastolic blood pressure (DBP), and pulse rate. This instrument

measures blood pressure from 0 to 300 mmHg and pulse rates from 30 to 180 beats per minute. It provides diagnostic accuracy of ±3 mmHg for blood pressure and 5% for pulse rate. Two readings were taken with a five-minute gap, and their average was recorded. If the difference between the readings was greater than 5 mmHg, a third reading was taken and the average of the last two readings was used to calculate the participants' blood pressure (Özkan et al., 2024; Paini et al., 2022).

Ethiopia has adopted the Joint National Committee's seventh report (JNC7) definition of high blood pressure (HBP) (Chobanian et al., 2003) into its National Clinical and Programmatic Management of Major NCDs Guideline (Walelgne, Yadeta, Feleke, & Kebede, 2016). Participants' BP was categorized as SBP and/or DBP ≥120/80 mmHg, covering both pre-hypertension and HTN. HTN is defined as SBP/DBP of ≥140/90 mmHg, confirmed by a physician or if the individual is taking antihypertensive medication. Pre-hypertension is characterized by a SBP of 120-139 mmHg and/or a DBP of 80-89 mmHg (Chobanian et al., 2003. Newly diagnosed HTN refers to participants with a SBP/DBP of ≥140/90 mmHg and who were unaware of their condition prior to this study.

3.4.5.1.2. Fasting Blood Glucose, Glycated Hemoglobin, and Their Assessment

At the ART clinic, individulas were enquired concerning their food consumption, excluding water, for the 8 to 12 hours before their arrival.Those who had fasted were then asked to provide a blood sample for the measurement of their blood biochemical biomarkers. Participants who had eaten breakfast were advised to fast overnight (8–12 hours) and return either the following day or during their next scheduled ART clinic visit to provide their blood samples. A gel-based serum separator tube (SST) and ethylene-diamine-tetra-acetic acid (EDTA) test tubes were used to collect 4 to 5 milliliter (mL) of blood from each study participant. The blood collected in SST tubes was kept at room temperature (17-25°C) for a maximum of 20 minutes to allow for adequate clot formation and to prevent glycolysis (Al-Kharusi, Al-Lawati, Al-Kindi, & Mula-Abed, 2014; Bhargava, Singh, & Gupta, 2019; Dibbasey, Umukoro, & Bojang, 2024; Fernandez et al., 2013). It was then promptly centrifuged at 3000 rpm for 8-10 minutes and the serum was separated from the clots using a gel barrier. Each participant's serum was analyzed immediately to determine FBG. If there was a delay of one week or less before analysis, the samples were stored at -20°C in Nunc tubes labelling with participant's unique code. EDTA-anticoagulated blood samples were analyzed for

HbA1c. Due to limited reagent availability, HbA1c testing was prioritized for newly diagnosed T2DM cases (FBG ≥126 mg/dL), with a focus on case management. HbA1c blood samples from participants with FBG <126 mg/dL were biobanked at -70°C in the lab. Additionally, FBG was determined by hexokinase method, while the HbA1c was determined by turbidimetric inhibition immunoassay (TINIA) method. FBG and HbA1c reagents were obtained from Roche Diagnostics, Germany and laboratory analysis were done using the Cobas 6000 series biochemistry analyzer (Roche, Germany).

Hyperglycemia was classified according to guidelines from the American Diabetes Association (ADA), which have been adopted in clinical management protocols for major NCDs (Care, 2023; Committee & Committee:, 2022; Walelgne et al., 2016). Hyperglycemia was defined as FBG ≥100 mg/dL. T2DM was diagnosed based on FBG ≥126 mg/dL, self-reported history, current use of antidiabetic medication, or confirmation from medical records. Newly diagnosed T2DM cases identified during this study were defined as individuals with FBG ≥126 mg/dL, confirmed by repeat testing and HbA1c measurement for case management. Prediabetes or IFG was defined as FBG between 100 and 125 mg/dL.

3.4.5.1.3. Lipid Profile and its Assessment

Overnight fasting blood samples of the study participants was analyzed immediately to determine lipid profiles. If there was a delay of one week or less before analysis, the samples were stored at -20°C in Nunc tubes labeled with participant's unique code. TC was measured using the cholesterol oxidase phenol 4-amino-antipyrine-peroxidase (CHOD-PAP) method; TGs were measured by glycerol phosphate oxidase-p-aminophenazone (GPO-PAP) method. HDL-c and LDL-c were measured using direct homogeneous enzymatic assay method. All necessary reagents for these lipid profile analyses were obtained from Roche Diagnostics, Germany and laboratory analysis were performed using the Cobas 6000 series biochemistry analyzer (Roche, Germany).

Then dyslipidemia was defined as per the revised National Cholesterol Education Adult Treatment Panel (NCEP ATP) III guidelines as TC ≥200 mg/dl, HDL-c <40 mg/dl, LDL-c ≥130 mg/dl, TG ≥150 mg/dl and a TC/HDL-c ratio ≥5.0 (Detection & Adults, 2002).

3.4.5.1.4. Metabolic syndrome and its Assessment

MetS was defined according to the 2009 harmonized criteria by the JIS (Alberti et al., 2009). Diagnosis required at least three of the following: TGs ≥150 mg/dL or treatment for elevated TGs; HDL-c <40 mg/dL in males or <50 mg/dL in females, or treatment for low HDL-c; BP ≥130/85 mmHg, history of HTN, or use of antihypertensives; FBG ≥100 mg/dL, history of DM, or treatment for elevated glucose; and WC ≥94 cm in males or ≥80 cm in females.

3.4.5.2. Independent variables

This study explored a range of independent variables across multiple domains: (1) Socio-demographic and economic factors: sex, age, marital status, education level, place of residence, occupation, religion, and income; (2) Behavioral factors**:** history of alcoholism, smoking, and substance abuse; (3) Anthropometrics and body composition measures: body weight, BMI, fat mass, fat free mass, visceral fat, WC, HC, WHR, WHtR, and neck circumference (NC); (4) Clinical and other factors: history of opportunistic infections, TB infection and use of anti-TB medications, adherence rates, duration of ART use, types of first-line ART regimens prescribed, presence of comorbidities, family history of hypertension and diabetes, psychiatric conditions (e.g., anxiety, depression, and memory issues), dietary intake (FAV intake), physical activity levels, and any changes in ART regimens (e.g., switching).

3.4.5.2.1. Anthropometrics and body composition variables and their assessment

Anthropometric data, including Wt, Ht, NC, and WC, were measured using a non-stretchable measuring tape following the WHO STEPS approach (Consultation, 2008). Height was measured using a stadiometer (Seca, Germany) while participants stood barefoot, wearing light clothing. For accurate measurement, participants were positioned with their heels, buttocks, shoulder blades, and the back of the head in contact with the stadiometer. Participants' WC was measured at the level of the umbilicus while they were standing in a relaxed posture, wearing light clothing. Measurements were obtained at the end of a normal exhalation to ensure consistency. HC measurement was taken at the maximal circumference over the buttocks, with the measuring tape positioned horizontally. A non-stretchable measuring tape was used to measure both the WC and HC, which were taken in accordance with the WHO stepwise method and recorded to the closest 0.1 cm. In addition, WC was divided by HC to determine WHR, and WC by height to determine

WHtR (Organization, 2011). NC was measured while participants stood upright with their arms relaxed at their sides. The head was positioned in the Frankfort horizontal plane, and the measurement was taken at the midpoint of the cervical spine and the mid-anterior neck, perpendicular to the neck's long axis, just below the Adam's apple for males (M. Verma, Rajput, Sahoo, & Kaur, 2017).

Bioelectrical impedance analysis (BIA) was employed via an Omron analyzer (Omron HBF-514C: OMRON Healthcare Inc.,) (Omron, 2014) to measure or estimate body weight, fat mass (FM, in kg), body fat percentage (BFP), fat-free mass (FFM, in kg), visceral fat level (VFL), and percentage skeletal muscle mass. The Omron BIA has been demonstrated to have a high to a very high level of reliability (intraclass correlation coefficient = 0.874 for females and = 0.966 for males). Based on the correlation with Air Displacement Plethysmography (ADP), its validity has also been proven to be high (r = 0.897 for women and r = 0.942 for men) (Vasold, Parks, Phelan, Pontifex, & Pivarnik, 2019). In addition, the Omron BIA device showed high agreement with dual X-ray absorptiometry (DXA) for FM (r=0.94) and moderate agreement for total percent fat (r=0.8) and FFM (r=0.91) (Cruz Rivera et al., 2022). Prior to stepping barefoot onto the scale with their feet shoulder-width apart, participants' age, and height (in centimeters [cm]), and sex were entered into the device. Participants were asked whether they had engaged in any of the following activities: intense exercise, taking a bath or sauna, consuming alcohol, drinking large amounts of water, or eating. If they had not engaged in any of these activities within 2 hours, measurements were taken directly. If they had, the measurements were taken after a 2-hour waiting period, as these factors might interfere with the accuracy of the BIA measurement (Omron, 2014). Participants stood barefoot on the foot electrodes, ensuring their weight were evenly distributed on the measuring platform. While holding a pair of electrodes connected to the display unit, the analyzer transmit a very mild electrical current of 50 kHz and less than 500μA through the tissues. Participants were then asked to extend their arms in front of their chest and remain until all measurements were completed. Body fat and skeletal muscle mass were estimated by manufacturer's valid and reliable formulas (Vasold et al., 2019). BIA provides measurement of body weight, BFP, visceral fat levels and percentage skeletal mass, while BMI was calculated from weight and height of each individual. FM, FFM and skeletal mass were then computed via BMI and BFP as follows: FM = weight × (BFP/100) and FFM = weight − [weight × (BFP/100)]. The BMI was subsequently determined and classified as underweight, normal, overweight, or obese

based on the WHO classification (Organization, 2022). Abdominal obesity was defined as a WC ≥94 cm for males and ≥80 cm for females (Organization, 2011). Moreover, abdominal obesity is indicated by a WHtR ≥0.5 and a WHR >0.90 in males and >0.85 in women (Organization, 2011). The visceral fat values were classified as "normal" (1–9) or "high" (10–30) for simplicity. Additionally, BFP and percentage skeletal mass were categorized based on age and sex: BFP was categorized as "normal" or "high," and percentage skeletal mass was categorized as "low" or "normal to high" as per the Omron manufacturer's guideline (Omron, 2014).

3.4.5.2.2. Alcohol intake, smoking and khat use

Participants who used khat, alcohol or smoke at least once in the month before the study are considered current users. While respondents who have ever used alcohol, tobacco or khat are indicated by their lifetime usage of these drugs (Meressa, Mossie, & Gelaw, 2009). The participants' mental health problems were evaluated using a validated Amharic version of the Hospital Anxiety and Depression Scale (HADS), which includes anxiety, depression, and corresponding severity categories (Reda, 2011).

3.4.5.2.3. Fruits and vegetables consumption and Physical activity performance

Regarding FAV intake, participants were asked on the frequency and portion amounts of their FAV intake. The WHO recommends eating 5 servings of FAV per day, each weighing 80 grams. The WHO recommends 5 portions of FAV daily, with each portion weighing 80 grams (WHO, 2004).

The International Physical Activity Questionnaire short form (IPAQ-SF) was used to evaluate the participants' physical activity levels (Craig et al., 2003; Forde, 2018), which describes high to low physical activity performance levels. In order to categorize their responses, respondents were asked to indicate the days and times throughout the period of the previous seven days that they had exercised at three distinct intensities: low, moderate, and vigorous. Heavy lifting or digging are examples of strong intensity activities while carrying modest burdens or riding a bicycle at a steady pace are examples of moderate effort activities. Walking is an example of low-intensity activity. The total weekly physical activity was calculated by dividing the time spent when doing each type of exercise by the metabolic equivalent of task (MET) for energy expenditure. The METs for vigorous, moderate and low-intensity activities, respectively, are 8.0, 4.0, and 3.3 (Forde, 2018).

Then MET-minutes/week was calculated as *METs* x *minutes of physical activity performed* x *number of days of activity performed*. Finally, the physical activity status of the participants was classified into the following groups based on the total METs score calculation: low active (<600 METs-minutes/week), moderate-active (≥600 to <3000 METs-minutes/week), and high active (≥3000 METs-minutes/week).

3.4.5.2.4. Psychiatric conditions

To screen participants' anxiety and depression status, a validated Hospital Anxiety and Depression Scale (HADS) questionnaire was employed, and HADS was assessed using a validated Amharic language questionnaire (Ambaw, 2011; Reda, 2011). The HADS comprises a 7-item depression subscale (HADS-D) and a 7-item anxiety subscale (HADS-A), all of which are self-reported (Noguchi, Kamada, & Shrira, 2014; Sangalang & Gee, 2012). All questions were scored on a 4-point Likert scale to determine how frequently participants experience anxiety and depression. A score of ≥11 on either subscale were considered severe depression or anxiety, a score of 8-10 borderlines, and a score of 0-7 normal (Ambaw, 2011; Reda, 2011).

3.4.6. Data collection tools and procedures

The questionnaire for data collection was initially created by adapting the WHO stepwise approach (Riley et al., 2016; WHO, 2008) and a thorough review of existing published literature. This comprehensive questionnaire addressed various aspects, including sociodemographic, economic, anthropometric, lifestyle, behavioral and clinical variables. To ensure accuracy and consistency, the questionnaire was initially developed in English and then translated into Amharic by a qualified bilingual expert. An interviewers (trained nurses working in the ART clinics) used a pretested Amharic version of the questionnaire to collect all the necessary information from the study participants through face-to-face interviews. In addition, information regarding the length of HIV infection, the baseline WHO clinical stage, the functional status of participants at the baseline, the presence of TB infection or use of TB prophylaxis treatment and use opportunistic infections prophylaxis treatment were explored from participants' medical records. Along with these, details on HIV and ART medications, presence of any comorbid conditions and other pertinent information also were obtained from each participant medical chart.

3.4.7. Statistical analysis

After the data was cleaned and coded, it was entered into Epi Data version 3.1 and later exported to SPSS version 27.0 for the purpose of statistical analysis. Categorical variables were summarized by frequency, while continuous variables were described using means with standard deviations (SDs) or medians with interquartile ranges (IQRs) as appropriate. In cases where continuous variables were skewed, a transformation was performed, employing either a logarithmic or square root approach. To assess multicollinearity among the independent variables, the variance inflation factor (VIF) was calculated using multiple linear regression analysis. A VIF value lower than 10 was considered acceptable, and this criterion was utilized to select the candidate variables for the final model (Chennamaneni, Echambadi, Hess, & Syam, 2016). The model's fit was evaluated with the Hosmer–Lemeshow test, where a p-value higher than 0.05 indicates a good fit. The differences among health facilities were minimal, reflected by an intraclass correlation coefficient (ICC) of less than 5%, suggesting a minor impact at the facility level (Koo & Li, 2016). As a result, a binary logistic regression model was employed for the analysis. Independent variables that had a p-value of 0.25 or lower from the bivariable analysis, along with other relevant variables identified in the literature were included into the multivariable analysis (Bursac, Gauss, Williams, & Hosmer, 2008a, 2008b). AORs with 95% CIs were used to assess the presence and strength of significant associations, with statistical significance set at $p < 0.05$.

3.5. Description of Methods for Evaluating the Influence of Lifestyle Modification Counselling on Body Weight and its Composition

This randomized controlled trial was conducted between January 5, 2023, and May 30, 2024, and was retrospectively registered in the Thai Clinical Trials Registry (TCTR20240905007) on September 5, 2024.

3.5.1. Study population

The study population were adult PLWH, aged between 18 and 65 years, who were classified as overweight and obese (BMI ≥25kg/m²) and were receiving first-line ART at healthcare facilities in Hawassa City Administration.

3.5.2. Sampling size determination

The sample size calculation for this trial was conducted via OpenEpi software version 3.01 (https://www.openepi.com/Menu/OE_Menu.htm), which considering the outcome variable of body weight change following lifestyle counselling. The calculation was performed using a 95%CI and a power of 80%. At the three-month evaluation, the intervention group had an average body weight of 85.6 kg (±15.96), which represented a mean weight loss of 4.09 kg from the baseline. On the other hand, the control group had an average weight of 94.02 kg (±14.96), showing a mean weight gain of 0.65 kg from baseline (Kucharska et al., 2018) (Table 3). The initial sample size was determined to be 106 but was adjusted to 132 with considering a 20% attrition rate. As a result, 66 participants were assigned to each study group with randomization based on their arrival according to the ART clinic follow-up schedule.

Table 3 Sample size calculation for intervention study by using OpenEpi software

Sample Size For Comparing Two Means				
Input Data				
Confidence Interval (2-sided)		95%		
Power		80%		
Ratio of sample size (Group 2/Group 1)		1		
	Group 1		***Group 2***	***Difference****
Mean	85.6		94.02	-8.42
Standard deviation	15.96		14.96	
Variance	254.722		223.802	
Sample size of Group 1		53		
Sample size of Group 2		53		
Total sample size		106	20% attrition	

3.5.3. Inclusion and exclusion criteria

3.5.3.1. Inclusion criteria

The study enrolled PLWH who were overweight and obese (BMI ≥25kg/m^2), aged 18 to 65 years and had been on ART at least for 12 months after the adoption of the test-and-treat in Ethiopia. Eligible participants included those with a baseline physical activity level of less than 600 metabolic equivalents of task in minutes per week (METs-min/wk), who had been on first-line ART, maintained viral suppression and were free of opportunistic infections during the intervention. They were receiving a first-line regimens consisting of two N(t)RTIs in combination with either EFVor DTG.

3.5.3.2. Exclusion criteria

Participants who had received formal dietary or physical activity counselling or had participated in organized nutrition and physical activity programs within the 6 months prior to this study were excluded. In addition, individuals with a history of pulmonary or cardiac complications, neurological problems, musculoskeletal disorders, confirmed thyroid disease, uncontrolled hypertension and physical conditions that restricts the ability to engage in physical activity, pregnancy at any point during the study and those with chronic liver and/or renal diseases. In addition, the study excluded individuals practicing religious fasting during the study period such as the Great Ethiopian Orthodox Fast or Muslim Ramadan, along with those who did not meet eligibility criteria.

3.5.4. Study variables

3.5.4.1. Outcome variables

Weight and body composition variables [weight, BMI, WC, HC, body fat percentage (BFP), fat mass (FM), fat free mass (FFM), skeletal muscle percentage and visceral fat level]. According to protocol, trained data collecors did variables measurement at the beginning of the intervention and at six months later. A stadiometer (Seca, Germany) was used to measure the body height of each participant. During the measurement, participants were instructed to remove their shoes and hairpins. The WC of participants was measured at the level of the umbilicus using a non-elastic measuring tape, with participants standing in a relaxed posture and ensuring no pressure was

applied to the body surface. The measurement was recorded to the nearest 0.1cm. The HC was taken at the maximum circumference of the buttocks, typically to the nearest 0.1cm. BIA analyzer (Omron HBF-514C) was used to measure body weight (in kg), FM (in kg), BFP, FFM (in kg), VFL (1–30 range), and percentage skeletal muscle (Omron, 2014). The study primarily focused on change in body weight and its composition, which were measured six months after the provision of lifestyle modifications counselling. Weight change was evaluated as both the absolute loss (in kg) from baseline and the percentage change from baseline. Percentage change from baseline for each individual was computed with the following formula: [((variable value at 6 months minus variable value at baseline)/variable at baseline) × 100]. Also we anticipated that the intervention group would achieve a minimum of 3% reduction in overall body weight after six months, relative to their baseline measurements.

3.5.4.2. Independent variables

The primary independent factor is lifestyle modification counselling (on dietary and physical activity). Other independent factors include sex, treatment regimens and baseline characteristics such as total energy intake, protein energy, and fat energy and lipid profiles.

The 24-hour recall dietary intake data were estimated via the standard measuring tools, common-size containers and pictorial displays that depicted food items and their portion sizes based on participants' responses. These estimates were computed using Ethiopian Food Composition Tables and Food-Based Dietary Guideline of Ethiopia (Gebru et al., 2023; Health & Institute, 1998; Institute, 1981). In addition, the dietary diversity score was assessed using the Individual Dietary Diversity Score (IDDS), while the frequency of food consumption was also evaluated (FAO, 2007). The IDDS is determined by adding up the number of food groups consumed within a 24-hour period. The resulting total score is then classified into three categories: a low IDDS indicates consumption of 1-3 food groups, a medium IDDS represents 4-5 food groups, and a high IDDS corresponds to 6 or more food groups (FAO, 2007). To achieve dietary adequacy, a diversified diet containing at least five food categories is required (Kennedy, Ballard, & Dop, 2010; Woldemariam, Yusuf, Beyen, & Yenit, 2015).

3.5.5. Randomization

A parallel-group, individual randomized controlled trial (RCT) with two groups was conducted to assess the effect of a 6-month lifestyle intervention (counselling) on weight and body composition among PLWH and a BMI of ≥25 kg/m². Participants were randomly assigned to one of two groups (intervention or control) in a 1:1 allocation ratio (Lee & Lee, 2021; Mohd Zaki et al., 2018; Vissers et al., 2008). Totally 132 participants with a BMI of ≥25 kg/m² were included with 66 in the intervention group (IG) and 66 in the control group (CG). The overall study has one intervention group and one control group. The allocation of participants to the IG or CG was done through simple randomization with both groups assessed over a 6-month period. Then the IG, which received personalized lifestyle modification counselling such as dietary, physical exercise and behavioural changes, while the CG, which continued with their usual routine care without additional counselling. Participants being randomized as they arrived to the ART clinics based on their follow up appointment. Participants were enrolled in the study between January 05, 2023 and May 30, 2024.

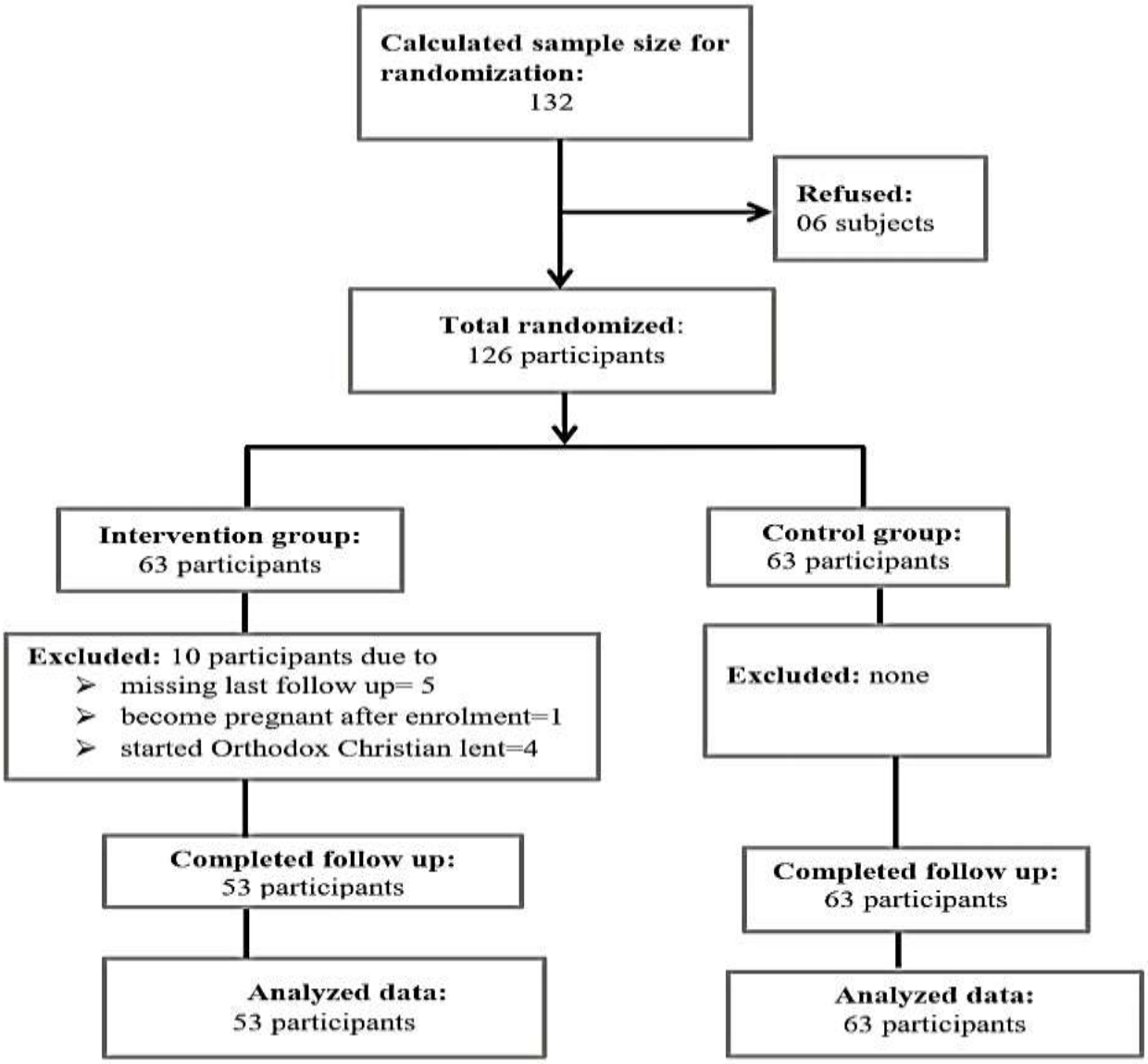


Figure 7 Schematic illustration of participants' enrolment in Randomized controlled trial

3.5.6. Intervention and Follow-up Procedures

The lifestyle modification intervention aimed to achieve and sustain a minimum 3% reduction from baseline weight, a threshold shown to yield clinically significant improvements in cardiometabolic risk factors (Ahmad Zamri et al., 2020; Jensen et al., 2014). The intervention included individualized counseling, beginning with an initial face-to-face session, followed by a minimum of two supportive counseling sessions conducted by phone. It included specific strategies such as modifying dietary intake habit, caloric restriction (reducing intake by approximately 500 kcal/day) and increasing physical exercise (doing at least moderate-intensity

physical activity). Nurse from the ART clinic who received counselling training for the study conducted the counselling sessions. The training materials for counsellor were developed by adapting guidelines and literature on managing bodyweight highlighting the benefits of healthy weight loss (Jensen et al., 2014; Yumuk et al., 2015). An initial 50–60 minute face-to-face counselling session focused on lifestyle changes was conducted for IG after all baseline study measurements were completed. Each participant in the IG received nutrition counselling from a counsellor who utilized motivational interviewing techniques under the oversight of the principal investigator. All intervention components were explained through counselling in Amharic language supported by pictures and photographs during face-to-face interviews and discussions. During the counseling sessions, participants were encouraged to implement lifestyle changes aimed at reducing their daily caloric intake by approximately 500 kcal. This energy deficit is typically achieved through a combination of dietary modifications, such as portion control, reducing consumption of high-calorie foods and beverages, and increasing the intake of nutrient-dense, lower-calorie options. Sustaining a daily caloric deficit of 500 kcal can create a negative energy balance, which over time leads to gradual weight loss by promoting the utilization of stored fat as an energy source. They advised incorporating whole grains, lean proteins, legumes and low-fat foods into their daily diets. Additionally, participants were encouraged to include locally available, fiber-rich foods, green vegetables (including Moringa *oleifera* leaves), and fruits in their diets. They also recommended avoiding overeating and limiting the consumption of refined grains, saturated fats, added sugars, high-calorie foods, fast foods and sugary or processed items.

Participants were also advised to increase physical activity and energy expenditure by engaging in 150-300 minutes of moderate-intensity exercise per week such as brisk walking, swimming, dancing, gardening, aerobics or biking; or 75-150 minutes of vigorous-intensity exercise, including running, aerobic dancing, cycling at speeds of 15km/h or faster or other similar activities. Alternatively, participants were also encouraged to engage in a combination of both moderate- and vigorous-intensity exercises. Additionally, they were strongly advised to minimize sedentary behaviors, such as prolonged sitting, television watching, computer use, or playing video games (Association; WHO, 2022). A brochure also developed in Amharic by adapting various guidelines and literature on weight management was provided to each participant in the IG (Jensen et al., 2014; Yumuk et al., 2015). The brochure included both narrative text and pictorial illustrations offering guidance on definition of obesity, side effects of obesity and benefits of weight loss

through dietary modifications, behavioural changes and the promotion of physical activity to support healthy weight loss. Furthermore, participants received a minimum of two remote supportive counseling sessions via phone calls, each lasting 20-30 minutes, during the first two months after randomization. These sessions were designed to support and encourage adherence to the recommended lifestyle changes. In contrast, the control group did not receive lifestyle counselling during the study but was instructed to attend the final assessment. Apart from the counselling, participants in the control group received the routine care from the ART clinics. Following the final assessment, they were provided with lifestyle counselling to enable them to achieve the anticipated benefits.

3.5.7. Data collection tools and procedures

The data collection questionnaire was developed by adapting various published literatures on weight management. It included sections on sociodemographic and socioeconomic factors, behavioural characteristics, clinical details, food frequency and 24-hour dietary recall. These data were collected through face-to-face interviews using a semi-structured questionnaire written in Amharic and administered by an interviewer. The 24-hour dietary recall was used to capture participants' food intake, assess dietary diversity, and calculate their average daily intake of total energy, macronutrients (carbohydrates, protein, and fat), and fiber. Baseline physical activity levels were assessed using the International Physical Activity Questionnaire short form (Craig et al., 2003; Matsudo et al., 2001). The study's outcome variables, such as body weight and body composition parameters, were assessed for both study groups at baseline and at the completion of the follow-up period. Moreover, participants' medical charts were reviewed to obtain supplementary information relevant to the study, including medical history, medications, diagnoses and other clinical data.

3.5.8. Statistical analysis

To minimize biases from non-completers, we conducted a per-protocol analysis, comparing study groups based solely on those who accomplished the study as planned. Categorical variables are presented as frequencies (percentages), while numerical variables are reported as means with standard deviations (SD) or medians with interquartile ranges (IQRs). The chi-square test was applied to assess the socio-demographic features of the participants and the independent t-test was

used to compare baseline characteristics between the study groups. Within-group changes in quantitative variables from baseline were analyzed using a paired t-test. While, o evaluate the differences in scores from pre-test to post-test, an independent t-test was employed for both the intervention and control groups. The weight loss was expressed as a percentage decrease from the baseline, calculated for each participant using the formula: [((value at 6 months - value at baseline) / value at baseline) × 100]. Dummy variables for demographic variables and weight loss were created and a comparison with the control group was performed. A linear mixed-effects model was also employed to assess the effect of counselling on body weight and body composition variables over time with an autoregressive error structure of order 1 (AR [1]). The model included time, intervention (counselling), DTG use, age, sex, duration since initiation of ART, and the time interval (Δtime) as fixed effects. The general model structure was Δweight/composition = β*time* + *β*intervention + β*other covariates + intercept (where β represents the regression coefficient for each variable). Each participant was treated as a random effect to account for individual variability. Multicollinearity was assessed using the variance inflation factor (VIF), with values <10 indicating no significant issue. Multiple linear regression, adjusted for baseline values was applied to assess changes in weight and body composition, as well as to determine a weight loss of at least 3% from baseline. Statistical significance was set at p value <0.05 with a 95%CI. Statistical analyses were performed using STATA version 17.0 (StataCorp LLC, College Station, Texas) and IBM SPSS Statistics version 27.0 (IBM Corp., Armonk, NY, USA).

3.6. Data and quality control

Before data collection, a proficient bilingual expert translated the English version questionnaire into Amharic. The Amharic version was then pretested on 46 cases outside the study site (Leku general Hospital) to assess clarity and make necessary revisions. A two-day training was conducted for six data collectors (nurses working in the respective health facilities) on data collection questionnaires, study ethics and participant consent, while two laboratory technologists were trained on blood collection procedures. The body weight instrument was calibrated daily using standard calibration tools, and the blood pressure apparatus was checked against a mercury-based sphygmomanometer. The principal investigator was responsible for supervising the data collection process, resolving any issues that emerged, and ensuring the questionnaires were

complete every day. Lastly, the data that was collected underwent a visual inspection and cleaning to assurance accuracy, consistency, and reliability in the data entry.

3.7. Ethical approval

The Institutional Review Board (IRB) of Addis Ababa University's College of Natural and Computational Sciences (CNS-IRB) approved the study on September 19, 2022, with the reference number: IRB/07/14/2022. Prior to the study's initiation, a support letter from the Hawassa City Administration Health Department was obtained and submitted to the medical directors' or heads of each participating health facility, and permission was secured. Participants were informed on the study's objectives, potential effects, and the significance of the data study. Written informed consent was obtained from all participants and they were informed about the right to withdraw or decline participation at any stage. To ensure data confidentiality, participant information was anonymous using codes, securely stored, and protected by password access. Participants with undiagnosed T2DM (FBG ≥126 mg/dL and HbA1c ≥6.5%) or hypertension (BP ≥140/90 mmHg) were promptly referred to clinicians/physicians at the respective ART clinics for appropriate management and follow-up care.

Chapter 4- *Results*

Chapter 4- Results

4.1. Effects of dolutegravir-based first-line ART on weight and BMI of adult PLWH in Hawassa city administration, Sidama Region

PAPER I

The paper was published in the journal of Annals of Medicine: **Tylors and Francis Journals group**: https://doi.org/10.1080/07853890.2023.2242250

This section (Chapter 4.1) presents the results of an investigation conducted on the impact of DTG-based first-line ART on weight and BMI among 524 adult PLWH who received follow-up care at health facilities in the Hawassa City Administration, Sidama Region. The study assessed changes in weight and BMI over 24 months among PLWH on first-line DTG-based therapy compared to those on first-line NNRTI-based therapies. The results highlighted the rate of ≥10% weight gain from baseline and its association with ART regimens and other contributing factors. The linear mixed effects analysis was conducted using STATA version 17.0 (StataCorp LLC, College Station, Texas), whereas other analyses were performed with IBM SPSS Statistics version 26.0 (IBM Corp., Armonk, NY, USA). The odds ratios for binary logistic regression, along with 95%CI were computed to identify factors associated with ≥10% weight gain.

The group that initiated first-line DTG-based regimens experienced significantly greater weight gain (8.6 kg vs. 4.95 kg, p<0.0001) and BMI increase (3.11 kg/m² vs. 1.84 kg/m², p<0.0001) over two years compared to the NNRTI-based regimen group. In contrast, the group that switched to DTG-based regimens showed no significant difference in weight (5.6 kg) or BMI (2.13 kg/m²) compared to the NNRTI-based arm (p>0.05). A significant interaction effect was observed between the DTG-based regimen and time in predicting changes in weight and BMI (β = 0.71; 95% CI: 0.34–1.07; $p < 0.0001$) and (β = 0.244; 95% CI: 0.10–0.39; $p = 0.001$), respectively. Initiation of ART with DTG-based regimens has been associated with at least a 10% body weight gain at two years (AOR = 1.9; 95% CI: 1.19–3.04). Age ≥40 years (AOR: 2.02; 95% CI: 1.35–3.02) and baseline factors such as weight <50 kg (AOR: 3.0; 95% CI: 1.86–4.84), advanced disease stages (AOR: 1.78; 95% CI: 1.1–2.86), and ambulatory or bedridden functional status (AOR: 2.0; 95% CI: 1.05–3.8) were also significantly associated with ≥10% weight increase.

4.2. The association between dolutegravir-based antiretrovirals and high blood pressure among adult PLWH on ART in Sidama Region

PAPER II

The paper was published in the journal of Therapeutic Advances in Infectious Diseases: **Sage Journals group:** https://doi.org/10.1177/20499361241306942

This section (Chapter 4.2) presents the results of a health facility-based cross-sectional study that examined the association between DTG-based first-line ART regimens and other factors contributing to elevated blood pressure among 444 adult PLWH who received follow-up care at health facilities in the Hawassa City Administration. The study focused on individuals who initiated first-line ART regimen after the adoption of the test-and-treat strategy and who had been on treatment for at least 12 months. The association between the outcome and explanatory variables was determined using binary logistic regression, with AOR and a 95%CI. Data entry done using EpiData 3.1, while IBM SPSS 27.0 (IBM Corp., Armonk, NY, USA) was used to perform statistical analysis.

The prevalence of HBP was 57.9% (95%CI: 52.5–62.4), with 40.5% classified as prehypertension and 17.3% as hypertension. Among participants with hypertension, 84.4% were newly diagnosed. Initiating ART with DTG-based regimens was associated with higher odds of HBP (AOR 5.9; 95% CI: 1.5–22.7) and switching to DTG-based regimens increased the odds of HBP (AOR 3.8; 95% CI: 1.1–13.9). Other significant factors associated with HBP included being male (AOR 2.6; 95% CI: 1.4–4.9), age >45 years (AOR 2.0; 95% CI: 1.2–3.4), high waist-to-height ratio (AOR 2.4; 95% CI: 1.1–4.9), inadequate vegetable intake (AOR 1.7; 95% CI: 1.0–2.7), inadequate physical activity (AOR 2.4; 95% CI: 1.1–5.4) and LDL-cholesterol (AOR 1.1; 95% CI: 1.0–1.2). Moreover, statistically significant interaction effects were observed between DTG based regimens and independent variables such as male sex, adequate physical activity, and BMIin predicting HBP and HTN.

4.3. Prevalence of hyperglycemia and its risk factors among adult PLWH on follow-up at the Hawassa city administration, Sidama Region

PAPER III

The paper was published in the journal of Endocrinology, Diabetes & Metabolism: **Wiley Journals group**: https://doi.org/10.1002/edm2.70054

In this section (chapter 4.3), the prevalence and predictors of hyperglycemia was investigated and identified among 443 adult PLWH who received follow-up care at health facilities in the Hawassa City Administration. The study focused on individuals who initiated first-line ART regimen after the utilization of the test-and-treat strategy and who had been on treatment for at least 12 months. AOR and 95% CIs were used to measure the strength of associations between risk factors and outcome. Data was entered in to EpiData 3.1 and and statistical analysis was done by IBM SPSS 27.0 (IBM Corp., Armonk, NY, USA).

Overall prevalence of hyperglycemia was 24.4% (16.7% prediabetes and 7.7% type 2 DM). Of the participants with DM, 82.3% were newly diagnosed. Age >50years (AOR 2.1; 95%CI 1.1–3.9), alcohol intake (AOR 2.1; 95%CI 1.02–4.2), obesity (AOR 3.2; 95%CI 1.3–7.9), high waist hip ratio (AOR 2.6; 95%CI 1.4–5.05), and LDL-cholesterol (AOR 2.2; 95%CI 1.02–4.6) were significant associated with hyperglycemia. While, factors significant associated with DM were alcohol intake (AOR 3.0; 95%CI 1.1–8.4), comorbidity (AOR 2.6; 95%CI 1.1–6.05), high waist circumference (AOR 7.5; 95%CI 1.3–43.3), high waist–hip ratio (AOR 4.1; 95%CI 1.02–16.2) and high-triglycerides (AOR 3.2; 95%CI 1.3–7.7). Dolutegravir based regimen did not show significant association with hyperglycemia. However, statistically significant interaction effects were observed between DTG-based regimens and both age > 50 years and BMI in predicting hyperglycaemia. In addition, sex-stratified analyses revealed significant interactions between DTG-based regimens and age > 50 years, overweight status, and elevated triglyceride levels in predicting hyperglycaemia.

4.4. The association between dolutegravir-based regimens and dyslipidemia among adult PLWH on follow-up at health facilities in Hawassa city administration, Sidama Region

PAPER IV

The paper has been submitted and accepted for publication in the journal of Atherosclerosis Plus: **Elsevier Journals group**

In this part (chapter 4.4), the prevalence and predictors of dyslipidemia were investigated among 450 PLWH who received follow-up care at health facilities within the Hawassa City Administration, Sidama Region. The study focused on individuals who had initiated a first-line ART regimen following the implementation of the universal test-and-treat strategy and who had been on treatment for at least 12 months. AOR and 95%CI were used to assess the strength of associations between risk factors and dyslipidemia. EpiData 3.1 was used for data entry, and subsequent statistical analysis was executed with IBM SPSS 27.0 (IBM Corp., Armonk, NY, USA).

Overall, 74.0% (95%CI: 69.8–78%) of participants had at least one lipid profile abnormality consistent with a diagnosis of dyslipidemia. The prevalence was 79.8% in males and 69.8% in females. The most common lipid abnormality was HDL hypocholesterolemia (66.4%), followed by high triglycerides (34.2%) and an elevated total cholesterol/HDL-cholesterol ratio (34.2%). Treatment initiating with DTG-based regimen (aOR: 4.8; 95%CI: 1.2–18.5), increased waist circumference (aOR: 1.06; 95%CI: 1.01–1.11) and neck circumference (aOR: 1.2; 95%CI: 1.06–1.5) were significantly associated with dyslipidemia.

4.5. Prevalence and Factors associated with Metabolic Syndrome among Adult PLWH on First-Line ART in Sidama Region

PAPER V

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In tis section (chapter 4.5), the prevalence of MetS and its associated factors were investigated among adult PLWH who had initiated first-line ART later the implementation of the test-and-treat strategy. The study focused on individuals who had been on treatment for at least 12 months. The strength of associations between risk factors and MetS was evaluated using AOR and 95% CI. Data were entered into EpiData 3.1, and statistical analysis was conducted using IBM SPSS 27.0 (IBM Corp., Armonk, NY, USA).

The prevalence of MetS was 36.4% (95%CI: 32.2–41.6), with low HDL cholesterol as the most frequent component observed in 368 (81.8%) participants. MetS was significantly associated with age >50 years (aOR: 2.9; 95%CI: 1.4–6.2), alcohol use (aOR: 2.7; 95% CI: 1.2–6.4), body mass index ≥25kg/m² (aOR: 3.7; 95%CI: 1.9–7.1), triglyceride/HDL-cholesterol ratio (aOR: 1.5; 95%CI: 1.3–1.7), family history of hypertension (aOR: 2.1; 95%CI: 1.1–3.8) and high waist-height ratio (aOR: 5.4; 95%CI: 1.8–15.9). DTG-based regimens did not show significant association with MetS ($p > 0.05$).

4.6. Effects of lifestyle modification counselling on body weight and body composition in overweight/obese adults On ART

PAPER VI

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In this section (chapter 4.6), the effect of counseling on lifestyle modification was evaluated in terms of its impact on body weight measures and body composition among 116 (53 intervention group and 63 controls) overweight/obese adults living with HIV on ART at health facilities in Hawassa city, Sidama Region. Body weight and composition variables were assessed at baseline and at the end of the intervention using the Omron Full Body Sensor Body Composition Monitor and Scale (Model HBF-514C). Primary outcomes were analyzed based on the per-protocol analysis principle. In this study, a primary outcome of at least a 3% reduction in overall body weight after six months, compared to baseline measurements, was used. This was calculated for each individual using the formula: [((weight at 6 months – weight at baseline) / weight at baseline) × 100]. The impact of lifestyle modification counselling on body weight and composition parameters was evaluated through linear mixed effects model and multiple linear regression analysis.

Over the six-month trial, the lifestyle modification counselling resulted in significant improvements in body weight (Δ = -1.4 kg, p=0.002), visceral fat (Δ = -0.53, p=0.006), fat mass (Δ = -2.16 kg, $p < 0.001$), and body fat percentage (Δ = -2.02%, $p < 0.001$) compared to the control group after the intervention period. In comparison to the control group, the intervention group experienced increases in lean mass (Δ = +0.673 kg, p = 0.068) and skeletal muscle percentage (Δ = +1.27%, $p < 0.001$). Additionally, lifestyle modification counselling significantly contributed to achieving at least a 3% weight loss from baseline (β = 0.158, p = 0.048).

Chapter 5- *General discussion*

Chapter 5- General discussion

5.1. Discussion

The widespread implementation of combination ART has significantly increased life expectancy among individuals living with HIV, however, cardiovascular and metabolic dysregulation are becoming serious challenges among PLWH (Lacson et al., 2017; Nsagha et al., 2015). PLWH on ART often experience an increased prevalence of cardiovascular disease (CVD) risk factors including type 2 diabetes mellitus (T2DM), overweight/obesity, hypertension (HTN) and dyslipidemia (Hemkens & Bucher, 2014; Lacson et al., 2017).

Compared to the NNRTI-based regimens, people on DTG-based first-line regimens gained significantly more weight. This result is in line with a number of observational studies and clinical studies that investigated at the same issue in various populations (Bourgi, Jenkins, et al., 2020; Sax et al., 2020; Venter et al., 2019). Weight increase after ART starting is frequently observed as an indicator of successful treatment and immunological restoration, which improves survival. However, significant weight gain might increase the risk of metabolic and cardiovascular complications (Kumar & Samaras, 2018).

The findings revealed an association between DTG-based first-line therapy and excessive weight gain, as a higher proportion of individuals on DTG regimens experienced weight gain compared to those on NNRTI-based therapy. This finding is similar with the reports of several clinical trials and cohort studies (Bourgi, Jenkins, et al., 2020; Sax et al., 2020; Venter et al., 2019). The mechanism behind integrase inhibitors-induced weight gain remains unclear, but it may be linked with the influence of melanocortin-4 receptor (MC4R), which regulates appetite and energy balance (Hill, Waters, & Pozniak, 2019). Moreover, the significant interaction between DTG-based regimens and time in predicting weight and BMI changes suggests a progressive increase in both parameters among individuals receiving DTG. The observed trends indicate that DTG use may be associated with sustained weight gain over time, raising concerns about potential long-term metabolic effects (Shamu et al., 2024; Tovar Sanchez et al., 2023).

Based on the WHO obesity criterion (BMI $\geq 30\ kg/m^2$), 10.2% of participants on DTG-based regimens and 5.3% on NNRTI-based regimens developed treatment-emergent obesity. However, this may underestimate the actual prevalence among Ethiopians, as applying the recently proposed population-specific BMI thresholds (BMI $> 22.2\ kg/m^2$ for males and

> 24.5 kg/m² for females) would likely result in higher estimates (Makeda Sinaga et al., 2018; M. Sinaga, Yemane, Tegene, Lidstrom, & Belachew, 2019).

The findings revealed that more than half of the participants had HBP, which aligns with results from a study conducted in Ghana (Iddrisu, Besing Karadaar, Gurah Junior, Ansu, & Ernest, 2023). However, the finding of this study was significantly higher than the 35% prevalence of HBP reported in Zambia (Hines et al., 2023). The higher rate in our study participants may be due to their prolonged engagement with newer regimens compared to the depicted study.

The prevalence of HTN in this study was 17.3%, which is consistent with several other studies conducted in Ethiopia and other African settings (Badacho & Mahomed, 2023; Brennan et al., 2023; Denu, Revoori, Buadu, Oladele, & Berko, 2024; Harimenshi, Niyongabo, Preux, Aboyans, & Desormais, 2022; Hines et al., 2023). DTG-based regimens were significantly association with HBP. This finding is consistent with previous studies, which found a significant association between DTG and HBP compared to NNRTI or PI-based regimens (Brennan et al., 2023; Kasoma Mutebi et al., 2023; Shamu et al., 2024). This might be attributed to increased weight gain in individuals on DTG-based regimens, which could contribute to rise in blood pressure (Brennan et al., 2023; Sax et al., 2020; Shamu et al., 2024).

In addition, men showed a higher rate of elevated blood pressure compared to women in this study, with indicating greater odds of developing HBP. These findings are consistent with studies showing a significant association between sex and increased blood pressure (Byonanebye et al., 2023; Kasoma Mutebi et al., 2023; Mbuthia et al., 2021). This may be due to estrogen, the primary female sex hormone, which helps protect against hypertension in females by promoting vasodilation, reducing inflammation, and modulating the RAAS, in contrast to males (Omotola, Legan, Slade, Adekunle, & Pendergast, 2019).

We found a significant association between low physical activity and HBP. This aligns with other studies reported similar findings (Badacho & Mahomed, 2023; Haile, Degelo, Adilo, Adem, & Gidisa, 2024). In addition, a significant association was observed between HBP and factors such as lipid profile, low vegetable intake and high WHtR. The findings are consistent with previous studies highlighting the association between elevated blood pressure and inadequate vegetable intake (Akpa et al., 2022), lipid profiles (Denu et al., 2024), and high WHtR (Choi JungRan, Koh SangBaek, & Choi EunHee, 2018).

The statistically significant interaction effects between DTG-based regimens and independent variables such as male sex, inadequate physical activity, and BMI in predicting HBP and HTN

suggest that the effect of DTG on blood pressure outcomes may be modified by these factors. Prior studies have similarly reported sex-specific and BMI-related variations in the cardiometabolic impacts of INSTIs, particularly DTG (Lake & Trevillyan, 2021; Sax et al., 2020; Venter et al., 2019). Additionally, physical inactivity may be linked to decreased insulin sensitivity, potentially worsening insulin resistance already observed in patients receiving DTG-based ART(Małkowska, 2024; Yaribeygi, Maleki, Sathyapalan, Jamialahmadi, & Sahebkar, 2021). Moreover, insufficient physical activity can impair vascular function by reducing endothelial responsiveness and increasing arterial stiffness, thus elevating systolic and diastolic blood pressure (Booth, Roberts, & Laye, 2012).

We found that the prevalence of hyperglycemia was 24.4%. This finding is higher than the rates reported in other studies, such as those conducted in Zambia (Shankalala et al., 2017) and Georgia (Borkowska et al., 2022). These inconsistencies may arise from variations in treatment duration, cut offs used for hyperglycemia (100 mg/dL vs. 110 mg/dL) and the differing effects of older versus newer ART regimens on glucose metabolism. We found substantial rate of T2DM, which was 7.7%. This is higher than the rate estimate reported for the general adult population in Ethiopia, which was 3.3% according to the IDF in 2021 (H. Sun et al., 2022) and 3.8% according to the WHO in 2016 (Roglic & Organization, 2018). The differences in diabetes prevalence between our study participants and the general population may be influenced by factors such as increased vulnerability to health complications, a compromised immune system and ART use, all of which may contribute to higher rates of prediabetes and T2DM.

This study did not identify a significant association between the use of DTG-based regimens and hyperglycemia. Conversely, other report suggested a potential association between the use of DTG-based regimens and an increased risk of hyperglycemia, possibly due to its impact on insulin sensitivity and glucose metabolism (Byereta et al., 2024). This inconsistency may result from variations in participants' demographics and potential interactions with lifestyle factors.

Obesity is identified as an independent factor associated with hyperglycemia in this study. The result corroborates existing literature, which has demonstrated a robust association between altered glucose metabolism and increased weight (Duguma & Gebisa, 2020; M. Jemal et al., 2023). In addition, dyslipidemia was associated with hyperglycemia. Similarly, several investigations have revealed a significant association of blood glucose levels with lipid

derangements (Ndagijimana, Nshimiyimana, Habyarimana, Izere, & Niyonzima, 2024; L. Wang et al., 2022).

The observed interaction effects between DTG-based regimens and BMI in predicting hyperglycaemia suggest that individuals with higher BMI may be more susceptible to DTG-associated glucose dysregulation. Sex-stratified analyses further indicate that these risks are amplified in subgroups with overweight status and elevated triglyceride levels. These findings align with previous studies showing that DTG may contribute to insulin resistance and metabolic disturbances, particularly in vulnerable populations (Erlandson et al., 2021; Lake et al., 2020; Sax et al., 2020).

Concerning dyslipidemia, almost three-fourth of adults with HIV had at least one dyslipidemia. This finding aligns closely with previous studies among PLWH in various African countries including Ethiopia (Ambisa Lamesa et al., 2023; Kigongo et al., 2024; Ombeni & Kamuhabwa, 2016). However, it was higher than the 23.6% pooled rate reported for the general adult people across Africa (Noubiap et al., 2018). The variations could be explained by several factors: differences in how various ART regimens affect lipid metabolism, the length of time individuals had been on ART and its influence on lipid metabolism. Low HDL was the most frequently observed lipid abnormality, present in 66.4% of participants or almost 7 out of 10 individuals. However, the rate was lower than that reported in several studies that ranged from 71.3% to 72.1% (Ambisa Lamesa et al., 2023; Asiki et al., 2015). These studies used <40 mg/dL for men and <50 mg/dL for women as cut-off points to define low HDL-c levels (Alberti et al., 2009), with the female cut-off being higher than the threshold recommended by the NCEP-ATP III guidelines for both sex (<40mg/dL) (Detection & Adults, 2002), which we used in our study. This difference in classification criteria may account for the higher prevalence rates observed in these studies compared to ours. Initiating treatment with DTG-based regimens increased the odds of dyslipidemia, with a risk nearly five times higher than NNRTI-based regimens. This finding corroborated by different studies (Byonanebye et al., 2021; Rebeiro et al., 2023). This may be attributed to the metabolic effects of DTG, which can alter lipid metabolism and potentially raise lipid profile compared to NNRTIs.

The overall prevalence of MetS in the study was 36.4%. This finding is higher than the rates reported in systematic reviews and cross-sectional studies conducted globally and in Africa, which ranged from 18.0% to 29.91% using IDF criteria (Ambachew et al., 2020; Girma et al., 2023; Nguyen et al., 2016; Tesfaye et al., 2014), 18.1 to 34.89% using ATP III criteria

(Ambachew et al., 2020; Girma et al., 2023; Nguyen et al., 2016; Tesfaye et al., 2014) and from13.9–33.1% using JIS (Amutuhaire et al., 2023; Bosho et al., 2018; Bowo-Ngandji et al., 2023; Kiama et al., 2018; Shidhaye et al., 2023). These discrepancies may be due to variations in diagnostic criteria, study periods, ART regimens and population characteristics. Low HDL-c was the most frequent component of MetS in this study, with a prevalence of 81.8%. However, our finding was higher than those of previous studies, which reported a low HDL-c prevalence rate of 64.1% in north-central Ethiopia (M. Jemal et al., 2023), and 72.1% in Uganda (Kigongo et al., 2024). Differences in treatment duration (Kigongo et al., 2024) and the varying effects of ART medications may also explain the observed variations in HDL-c level across studies.

Sex was not associated with MetS in this study, which is consistent with the reports from Nigeria (Muhammad et al., 2017) and Ethiopia (Jarso, Aman, & Megerso, 2024). In contrast, several similar studies conducted in PLWH (Benson M Hamooya, Lloyd B Mulenga, et al., 2021b; Tesfaye et al., 2014; Vargas-Pacherrez et al., 2020) indicated significant association between female sex and MetS. This might be due to hormonal differences, abdominal fat level, physical activity status and cultural factors, all of which may influence metabolic risk differently between sexs across studies. TG/HDL-c showed a significant association with MetS. The finding is consistent with results from other studies that reported similar associations between TG/HDL-c and MetS (Chen et al., 2015), highlighting a stronger association between TG/HDL-c and the occurrence of CVD (Flores-Guerrero et al., 2024). In addition, BMI and WHtR were significantly associated with MetS. Similar findings have been reported in other studies conducted in Ethiopia and elsewhere (Calza et al., 2017; Chen et al., 2015; Gebreegziabiher, Belachew, Mehari, & Tamiru, 2021; A. Jemal et al., 2023; Kiama et al., 2018; S. D. Mallya & Reddy, 2020; Tesfaye et al., 2014; Vargas-Pacherrez et al., 2020).

Concerning policies and strategies: Ethiopia has developed national strategies such as the National Food and Nutrition Strategy (FDRE, 2021), the Food-Based Dietary Guidelines (FDRE, 2022), the National major NCD Strategic Plan for 2020–2025 (FMoH, 2020) and the review on Sustainable Development Strategy (SDS) (FDRE, 2017). These policies emphasize comprehensive public health strategies such as the promotion of healthy dietary practices, enhancement of physical activity, and systematic screening and management of NCDs to proactively tackle malnutrition and the escalating burden of NCDs. However, the emerging cardiometabolic risks associated with newer first-line ART in PLWH require great attention,

as findings from this study reveal significant associations with a heightened cardiometabolic risks such as incidence of obesity, high blood pressure, hyperglycemia, dyslipidemia, and metabolic syndrome. In addition, the conditions strongly associated with modifiable risk factors such as physical inactivity, low vegetable intake, central obesity, elevated LDL cholesterol, and alcohol consumption. While current policy documents promote healthy diets and physical activity at the population level, more targeted guidance is needed to address these specific risks within HIV care settings. Furthermore, continued reliance on the WHO obesity threshold (BMI ≥30 kg/m²) may underestimate obesity-related risks in the Ethiopian population including PLWH. Recent evidence suggests that lower obesity threshold than those recommended by the WHO may be more appropriate for the Ethiopian population (Makeda Sinaga et al., 2018; M. Sinaga et al., 2019), highlighting the need to develop nationally relevant thresholds to enhance early risk identification and intervention.

Regarding intervention study, participants in the counselling group experienced a significant weight reduction over six months compared to the control group. This finding aligns with previous studies demonstrating similar effects of face-to-face, remote, or combined counselling interventions (Groeneveld, Proper, Van der Beek, & Van Mechelen, 2010; Lutes, Cummings, Littlewood, Dinatale, & Hambidge, 2017; Moncrieft et al., 2016; Van Wier et al., 2009). The intervention group demonstrated a significant decrease in body fat percentage, visceral fat, and fat mass compared to the control group. These results are consistent with previous research highlighting similar improvements in body composition following lifestyle interventions (Afifi, Hassan, Abdelrahman, El Sayed, & Salem, 2023; Batsis et al., 2022; Mendonça et al., 2022) and also align with studies conducted in PLWH (John et al., 2018; Ogalha et al., 2011). In addition, studies have shown improvements in skeletal muscle mass, with a significant increase in the intervention group compared to the controls (Fazliana et al., 2018; Mohd Zaki et al., 2018; Nishiguchi et al., 2014). Consistent with these findings, we observed a notable increase in skeletal muscle and fat free mass in the counselling group from baseline and compared to controls. The improved exercise and dietary modifications may support the development of skeletal muscle and FFM (Rejeski et al., 2019). The intervention significantly associated with a weight reduction of at least 3% from baseline. Similar studies have reported comparable effects on body weight (Group, 2013; Virtanen, Penttinen, Kautiainen, & Korhonen, 2021).

5.2. Strengths and limitations of the study

The present study has several strengths and limitations. As strengths, the study aimed to include participants from multiple ART-providing health facilities, offering valuable insights into cardiometabolic outcomes among PLWH. This study focused on adults who started ART following Ethiopia's adoption of test-and-treat strategy. This focus ensures that the findings are relevant to current treatment practices. The study included only PLWH who were on ART for at least 12 months, could be sufficient time to investigate the effects of ART on cardiometabolic health. Excluding individuals who had switched regimens multiple times could minimized the potential confounding effect of regimen changes. However, the study has some limits. Its cross-sectional design limits conclusions to associations, not causality. Relatively small number of participants receiving the NNRTI-based regimens due to the national roll out to DTG-based treatments made a little bit challenge to compare outcomes between these two groups. The reliance on self-reported datamay introduce the possibility of recall bias and the single-phase twice blood pressure measurement may not have captured fluctuations throughout the day or in different environments. The baseline data on food frequency, 24-hour dietary recall and physical exercise were self-reported, which may have introduced inaccuracies and response bias. Moreover, nearly one-fourth of participants in the intervention group reported economic constraints, which may have limited their access to a variety of healthy, diversified and fiber-enriched foods essential for supporting weight loss and management. The relatively short duration of the lifestyle counselling intervention also limited the ability to fully explore its long-term effects on body weight and composition.

Chapter-6 *Conclusion & recommendation*

Chapter-6 Conclusion and Recommendations

6.1. Conclusion

We aimed to to assess the burden and identify factors associated with cardiometabolic risks among adult PLWH receiving follow-up care at health facilities in southern Ethiopia. The findings indicated that excess weight gain is significantly higher among individuals on first-line ART regimens. Additionally, elevated blood pressure, hyperglycemia, dyslipidemia and MetS were prevalent among adult PLWH, most of whom were receiving first-line DTG-based regimens.

First-line DTG-based regimens led to greater increases in weight and BMI compared to the NNRTI-based regimen. Treatment initiation with first-line DTG-based regimens was significantly associated with a ≥10% increase in body weight from baseline. Other factors such as age and baseline factors like low weight, advanced disease stages and functional status were also associated with with ≥10% weight gain.

The prevalence of high blood pressure was significant with a substantial proportion classified as prehypertension and a notable portion as hypertension. Among those with hypertension, most were newly diagnosed. Starting ART with first-line DTG-based regimens and switching to these regimens were associated with high blood pressure. Non-modifiable risk factors included being male and older age, while modifiable factors such as a high WHR, low vegetable intake, low physical activity and elevated LDL-cholesterol were also associated high blood pressure.

The prevalence of hyperglycemia was markedly high, with a significant proportion of participants being newly diagnosed with diabetes. Factors such as older age, alcohol consumption, obesity, WHR and elevated LDL-cholesterol were significantly associated with hyperglycemia. While, alcohol use, comorbidities, and high WC, WHR, and elevated triglycerides were associated with diabetes.

A significant proportion of participants had dyslipidemia, with higher prevalence in males. The most frequent abnormality was low HDL cholesterol. Treatment initiation with DTG-based regimens, along with high WC and NC were significantly associated dyslipidemia.

The prevalence of MetS was high among adult PLWH, with higher rates observed in females. The most common component was low HDL cholesterol. Factors associated with MetS were older age, alcohol use, higher BMI, high TG/HDL cholesterol ratio, family history of hypertension and high WHtR.

The six-month lifestyle modification counselling for individuals with a BMI ≥25 kg/m² resulted in significant improvements in body weight, visceral fat, fat mass, and BFP in the intervention group compared to the control group. In addition, the intervention group demonstrated increases in FFM and skeletal muscle percentage. Counselling was also significantly associated with a reduction in weight of at least 3% from baseline.

6.2. Recommendations

Based on the findings, the following recommendations are proposed to enhance metabolic health outcomes in adults living with HIV, optimize ART practices, inform policy development and guide future research.

Recommendations for PLWH on ART

- Engage in at least 150 minutes of moderate-intensity physical activity per week (e.g., brisk walking, cycling, or household activities).
- Incorporate locally available, fiber-rich foods (such as whole grains, legumes, fruits, and vegetables) into their daily diet.
- Maintain regular meal patterns and adopt self-initiated screening practices for cardiometabolic risks such as blood pressure, blood glucose, lipid profile and others.

For programme implementers/ service providers

- Targeted training and refresher programs for healthcare workers in ART clinics are required
- Ensure nationwide implementation and quality assurance of the integrated services
- Ensure routine monitoring and accurate documentation of anthropometric and cardiometabolic parameters during ART visits to support clinical decision-making
- Consistent delivery of structured lifestyle counselling for PLWH within HIV care service is required

For policy makers

- Strengthen health education and awareness programs focused on HIV transmission, and strengthen early HIV diagnosis and treatment services to effectively reduce HIV transmission rates.
- Strengthen sustainable health information dissemination systems to promote healthy lifestyles and improve cardiometabolic awareness among PLWH.
- Allocate adequate resources to ensure the effective delivery of cardiometabolic health services within ART clinics.

For Future Research:

- Conducting long-term studies is essential to better understand the cardiometabolic effects of DTG-based regimens and to assess the progression of cardiometabolic complications over time.
- Exploring the interplay between genetic predispositions, and environmental factors affecting metabolic health in diverse PLWH in sex stratification. This would provide valuable insights for personalized treatments and improved health outcomes.

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Publications and Manuscripts Submitted to Peer-Reviewed Journals

PAPER I

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RESEARCH ARTICLE

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Effect of dolutegravir-based first-line antiretroviral therapy on weight and body mass index among adult people living with HIV on follow up at health facilities in Hawassa city administration, Southern Ethiopia: a retrospective cohort study

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ABSTRACT

Background: The nature and burden of weight gain associated with antiretroviral treatment (ART) using a combination of Tenofovir disoproxil fumarate, lamivudine and dolutegravir (TLD) among people living with HIV (PLWH) has not been thoroughly investigated in Ethiopia. Therefore, this study aimed to evaluate changes in body weight and body mass index (BMI) in adults who initiated TLD or switched to TLD compared to those who received a non-nucleoside reverse transcriptase inhibitor (NNRTI)-based therapies.

Methods: A retrospective cohort study was conducted among adult PLWH who had been receiving ART between February 2017 and October 2022 in Hawassa city administration, Sidama region. Linear mixed-effects model was used to examine BMI and body weight trends over time, while a binary logistic regression was performed to identify factors associated with $a \geq 10\%$ weight gain.

Results: A total of 524 adult PLWH with a median age of 35 (interquartile range: 30–41) years were included. TLD-initiated arm experienced significantly greater mean weight (8.6 kg vs. 4.95 kg, $p < 0.0001$) and BMI (3.11 kg/m^2 vs. 1.84 kg/m^2, $p < 0.0001$) increase than the NNRTI-based arm at two years. However, the switched arm showed no significant difference in weight (5.6 kg) and BMI (2.13 kg/m^2) compared to the NNRTI-based arm ($p > 0.05$). There was a significant interaction effect between ART regimens and time in predicting weight and BMI gain ($p < 0.01$). Initiating ART with TLD had higher odds of ≥10% body weight gain at two years (adjusted odds ratio [AOR]: 1.9; 95% CI: 1.19–3.04). Other baseline factors such as age ≥40 years (AOR: 2.02; 95% CI: 1.35–3.02), weight <50kg (AOR: 3.0; 95% CI: 1.86–4.84), advanced disease stages (AOR: 1.78; 95% CI: 1.1–2.86) and ambulatory-bedridden functional status (AOR: 2.0; 95% CI: 1.05–3.8) were also associated with ≥10% weight gain.

Conclusion: Initiating ART with TLD was significantly associated with greater weight and BMI gain than the NNRTI-based regimens. Therefore, the cardio-metabolic implications of weight gain after the TLD initiation in this population should be monitored and thoroughly investigated.

KEY MESSAGES

- A significant interaction effect was observed between ART regimens and time in predicting weight and BMI gain.
- Starting ART with TLD was associated with a significant weight gain and treatment-emergent overweight/obesity than the NNRTI-based therapies.
- ART initiating with TLD had 1.9 times higher odds of >10% body weight gain than the NNRTI-based therapies

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Introduction

Weight gain after starting antiretroviral treatment (ART) is common, specifically in people with very low CD4+ count or lower pre-ART body mass index (BMI) [1]. Weight gain following ART initiation is frequently interpreted as evidence of treatment success and nutritional rehabilitation and it is associated with increased survival [2] and immunologic reconstitution [1]. A substantial weight gain which is associated with ART, on the other hand, may increase the risk of comorbidity with metabolic and cardiovascular diseases [3]. In particular, obesity is a significant risk factor for cardiovascular disease [4], type 2 diabetes [5], sleep apnea, psychiatric problems, several musculoskeletal diseases, and some malignancies [6].

In terms of ART regimens, integrase strand transfer inhibitors (INSTIs) are now recommended as preferred first- and second-line ART modalities for people living with HIV (PLWH) [7], due to their strong barrier to resistance and higher tolerability [7,8]. However, recent studies showed that excess weight gain or clinical obesity was more frequent among individuals taking INSTI-based ART classes, particularly dolutegravir (DTG) compared to individuals in other antiretroviral classes [9]. In addition, factors like African descent, female gender, and high pre-treatment HIV viral load or low baseline CD4+ count were also associated with moderate to excess weight gain [10]. Ethiopia changed its guideline to use INSTI-based combinations as preferred first- and second-line ART regimens in 2018 [11] following the World Health Organization (WHO) recommendation [12]. However, only limited data are available concerning the effect of INSTIs-based ART regimens on body weight and BMI in the Ethiopian population. As a result, we investigated whether initiating or switching to INSTI-based first-line therapy is associated with weight gain compared to non-nucleoside reverse transcriptase inhibitor (NNRTI)-based first-line therapies among adult PLWH after 24 months of treatment follow-up.

Materials and methods

A retrospective cohort study was conducted among adult PLWH who had been receiving antiretroviral medications between February 20, 2017 and October 30, 2022. We collected data from seven public and private health facilities that provide ART service for PLWH in Hawassa city administration, Sidama regional state. These health facilities were Adare General Hospital, Alatyon Hospital, Hawassa University Comprehensive Specialized Hospital (HUCSH), Hawela-Tulla Hospital, Bushulo Health Center, Millennium Health Center, and Tulla Health Center. The medical records of the study participants were accessed from November 01 to December 15, 2022.

Inclusion criteria

All PLWH who were at least 18 years of age, had been on first-line ART for at least two years and had started ART for the first time after Ethiopia implemented the WHO test-and-treat strategy (February 2017) [12,13] were included. Only adult PLWH who had suppressed HIV-1ribonuclic acid or (HIV-1 RNA <1000 copies/mL after twelve months of ART initiation) were eligible for the study. Regarding ART regimens, the following treatment arms were considered for weight and BMI analysis: [1]. Patients who had started treatment with Tenofovir disoproxil fumarate (TDF) plus lamivudine (3TC) and DTG (TLD) at the baseline and stayed on the same regimen for 24 months and had at least five of the consecutive weight data starting from the baseline (TLD arm) [2]. Those who started treatment with two nucleos(t)ide reverse transcriptase inhibitors (N(t)RTIs) plus either efavirenz (EFV) or Nevirapine (NVP) at the baseline and then switched to the TLD regimen within 24 months, and had received the initial EFV/NVP-based regimens for at least six months prior to switching and/or at least one post-switch weight data during the 24-month follow-up (switch arm) [3]. While the comparison group included individuals who initiated treatment with two N(t)RTIs plus either EFV or NVP at the baseline, remained on the same regimens and had at least five weight data from the baseline throughout the 24-month follow-up (NNRTI-based arm).

Exclusion criteria

Adults who initiated ART before the start of the test-and-treat strategy, which means those who initiated ART before February 2017, those with poor adherence to ART therapy, those transferred in from other health facilities, those who switched to TLD before six months of therapy, and women who were pregnant at any point during 24-month follow up were all excluded from the study. In addition, participants whose follow-up records did not include the baseline and follow-up weight data for at least 24 months and those who were lost to follow-up or died before 24 months were also excluded. For more information, the inclusion and exclusion of the study participants are indicated in the flow chart (Figure S1).

Data collection tools and procedures

A standard checklist was used to collect the information from participants' medical records. This checklist was developed using the ART initiation and follow-up form used in the ART clinics. The following data were collected using this checklist: socio-demographic factors such as age, gender, marital status, religion, residence, occupation, and educational levels; clinical information such as duration since HIV diagnosis, duration of ART experience, baseline WHO disease stage, functional status, history of tuberculosis (TB) infection, type of TB infection, presence of opportunistic infections (OIs) other than TB, treatment with anti-TB, use of TB prophylaxis treatment (TPT), opportunistic infections prophylaxis treatment (OPT), comorbid health problems, baseline ART regimens, modification on ART regimens (switching); anthropometric measurements such as weight over 24 months and height values of the individuals. All compulsory data were collected by health professionals with the critical review of each participant's medical chart under the supervision of the principal investigator.

Outcome assessment

Percentage weight gain from baseline was calculated for each individual and adapted to (weights at x-month minus weight at baseline/weight at baseline) x100 [14]. In addition, moderate weight gain was defined as a 5 to <10% increase in weight from baseline, whereas excess weight gain was defined as $a \geq 10\%$ increase in body weight or BMI by ≥1 kilogram/square meter (kg/m^2) at 12 or 24 months of treatment follow up [9,10,15–17]. For individuals who had recorded height values, BMI was calculated as weight (kg) divided by the square of height in meters (m^2) and then divided into four categories as follows: underweight (<18.5 kg/m^2), normal weight (18.5–24.9 kg/m^2), overweight (25.0–29.9 kg/m^2), and obese (≥30kg/m^2) [18,19].

Ethical approval

The Institutional Review Board at the College of Natural and Computational Sciences (CNS-IRB) at Addis Ababa University granted ethical approval for the study (approval No: IRB/07/14/2022) and waived the requirement to obtain informed consent as this study used de-identified secondary data from medical records. A letter of approval received from Addis Ababa University was submitted to the Hawassa city administration's health department office for evaluation and writing of support letters for each study health facility. Then, an official letter of support, received from the Hawassa city health department office, was submitted to the Medical director's office of the seven health facilities to obtain an official approval for data collection. In addition, the study complied with the standards of the Helsinki Declaration and its subsequent amendments. The confidentiality of study participants' personal information was highly preserved.

Statistical analysis

Means with 95% confidence intervals (CI) or medians with interquartile ranges (IQRs) were utilized as summary measures for continuous variables. Baseline demographic and clinical characteristics across the ART treatment arms were evaluated using the Pearson $\chi 2$ test, student t-test, or one-way ANOVA as appropriate. The effect of treatment with a DTG-based first-line regimen on weight/BMI over time was analyzed using linear mixed-effects model with autoregressive error structure of order 1 treating each participant as a random effect and adjusting for age, sex, TB coinfection and time. The main outcome of interest in the present study was weight gain of ≥10% over the 24-month ART follow-up. The effect of DTG-based first-line regimens on ≥10% body weight gain was investigated using multivariable binary logistic regression with adjusting for the effects of age at ART commencement, sex, duration since HIV diagnosis, baseline weight, TB infection, baseline WHO clinical stage, baseline functional status, TPT, and OPT. All covariates with a p-value of < 0.25 in bivariate analysis were included in the multivariable analysis except for sex. An alpha threshold of 5% was set for statistical significance. Stata version 17.0 (StataCorp LLC, College Station, Texas) was used for the linear mixed effects analysis, while other analyses were done using IBM SPSS Statistics version 26.0 (IBM Corp., Armonk, NY, USA).

Results

Baseline characteristics of the study participants

A total of 6,300 adults were receiving ART at seven health facilities during the time of data collection. Of these, 524 adults met the inclusion criteria for body weight analysis. Also, only 482 (92%) of the 524 adults had recorded height values and BMI was calculated for them. The study participants had a median age of 35 (IQR: 30–41) years at baseline and 56.7% (297/524) were females (Table 1).

Table 1. Baseline socio-demographic features of the study population.

Variable	Total	ART regiments at baseline		P-value
		NNRTI-based arm	TLD arm	
	n = 524	*n* = 367	*n* = 157	
Gender				
Female	297(56.7)	213(58.0)	84(53.5)	0.337
Male	227(43.3)	154(42.0)	73(46.5)	
Age in years, median(IQR)	35(30–41)	35(29–42)	35(30–40)	0.617
Marital status	*(n = 485)*	*(n = 350)*	*(n = 135)*	
Single	76(15.7)	55(15.7)	21(15.5)	0.88
Married	262(54)	189(54)	73(54.1)	
Divorced	83(17.1)	62(17.7)	21(15.5)	
Widow/widower	64(13.2)	44(12.6)	20(14.8)	
Residence	*(n = 509)*	*(n = 359)*	*(n = 150)*	
Rural	78(15.3)	51(14.2)	27(18.0)	0.279
Urban	431(84.7)	308(85.8)	123(82.0)	
Religion	*(n = 493)*	*(n = 357)*	*(n = 136)*	
Orthodox	185(37.5)	132(37.0)	53(39.0)	0.899
Protestant	256(51.9)	186(52.1)	70(51.5)	
Muslim	44(8.9)	34(9.5)	10(7.3)	
Catholic	5(1.0)	3(0.8)	2(1.5)	
Others	3(0.6)	2(0.6)	1(0.7)	
Occupation	*(n = 321)*	*(n = 228)*	*(n = 93)*	
Employed*	202(62.9)	140(61.4)	62(66.7)	0.087
No job	18(5.6)	14(6.1)	4(4.3)	
Daily laborers	16(5.0)	9(3.9)	7(7.5)	
Housewife	68(21.2)	54(23.7)	14(15.0)	
Farmers	10(3.1)	7(3.1)	3(3.2)	
Students	6(1.9)	4(1.7)	2(2.1)	
Commercial sex workers	1(0.3)	0(0.0)	1(1.1)	
Education	*(n = 489)*	*(n = 351)*	*(n = 138)*	
Unable to read and write	51(10.4)	39(11.1)	12(8.7)	0.061
Primary level (grade 1–8)	143(29.2)	112(31.9)	31(22.5)	
Secondary (grade 9–12)	185(37.8)	130(37.0)	55(39.8)	
College and above	110(22.5)	70(19.9)	40(29.0)	

Values presented in number (%) unless otherwise indicated; *, (include government, private and self-employed); IQR: interquartile range; ART: antiretroviral therapy; TLD: Tenofovir disoproxil fumarate plus lamivudine and dolutegravir; NNRTI-based: nucleos(t)ide reverse transcriptase inhibitors plus non-nucleoside reverse transcriptase inhibitor.

Baseline anthropometric and clinical characteristics of the study population

Ninety-seven (18.5%) PLWH had a history of tuberculosis infection, 72 (74.2%) of them had pulmonary tuberculosis, and 25 (25.8%) had extra-pulmonary tuberculosis. Likewise, 47(8.9%) subjects had opportunistic infections other than tuberculosis (Herpes zoster ($n = 29$), pneumocystis pneumonia ($n = 4$), toxoplasmosis ($n = 4$), and candidiasis infection ($n = 10$)). Of the 524 adults, 70% (367/524) initiated ART with the NNRTI-based regimens, while 30% (157/524) initiated the TLD regimen. Of those who initiated the NNRTI-based regimens, 98.4% received TDF + 3TC + EFV, while 1.1%, 0.3%, and 0.3% received Zidovudine (ZDV) + 3TC + EFV, TDF + 3TC + NVP and abacavir (ABC)+3TC + EFV, respectively (Table 2). One hundred seventy-nine (34.1%) participants continued receiving the NNRTI-based regimens for 24 months; while 35.9% (188/524) adults were switched from the NNRTI-based regimens to TLD regimen before 24 months of treatment as per the WHO guidelines. Forty-two out of 524 (8.0%) adults had no documented height values to calculate the BMI and only 482 adults were considered for the BMI analysis. Of the 482 participants, 69.5% (335/482) initiated ART with the NNRTI-based regimens, while the remaining 30.5% (147/482) initiated the TLD regimen. About 33.8% (163/482) participants continued receiving the NNRTI-based regimens; while 35.7% (172/482) were switched from NNRTI-based regimens to the TLD regimen as per the WHO directions.

Body weight and BMI increase after ART initiation

Overall, body weight increased by 4.6 kg (95% CI: 4.06–5.15 kg) at 12 months, and 6.3 kg (95% CI: 5.65–6.94 kg) at 24 months. At 24 months, participants who started TLD gained a mean of 8.6 kg (95% CI: 7.35–9.92 kg) compared to 4.95 kg (95% CI: 3.87–6.02 kg) gain in the NNRTI-based arm ($p < 0.0001$). Weight gain in the switched arm (5.6 kg; 95% CI: 4.65–6.61 kg) was greater than weight gain in the NNRTI-based arm, but the difference was not statistically significant ($p > 0.05$) (Figure 1A).

Similarly, the BMI increased by 1.7 kg/m^2 (95% CI: 1.47–1.89 kg/m^2) at month 12, and 2.3 kg/m^2 (95% CI:

Table 2. Baseline anthropometric and clinical features of the study population.

Parameter	Total $n=524$	ART regiments at baseline: NNRTI-based arm $n=367$	ART regiments at baseline: TLD arm $n=157$	p value
Duration since HIV diagnosis(months)*	48(37–56)	53(47–60)	34(28–37)	***<0.0001***
Duration since ART start (months) *	46(36–54.7)	51(45–58)	34(28–37)	***<0.0001***
Weight (kg)#	58.6(57.4–59.6)	58.8(57.5–60)	58.4(56.4–60.3)	0.74
BMI(kg/m^2)#	21.5(21.1–21.8)	21.7(21.1–22.1)	21.1(20.5–21.7)	0.161
BMI (kg/m^2)	$n=482$	$n=335$	$n=147$	
Underweight (<18 kg/m^2)	109(22.6)	72(21.5)	37(25.2)	0.289
Normal weight (18–24.9 kg/m^2)	279(57.9)	193(57.6)	86(58.5)	
Overweight (≥25 kg/m^2)	82(17.0)	59(17.6)	23(15.6)	
Obese	12(2.5)	11(3.3)	1(0.7)	
WHO clinical stage				
Stage-I	215(41.0)	165(45.0)	50(31.8)	***0.022***
Stage-II	132(25.2)	88(24.0)	44(28.0)	
Stage-III	119(22.7)	73(19.9)	46(29.3)	
Stage-IV	58(11.1)	41(11.2)	17(10.8)	
Functional status				
Working	447(85.3)	315(85.8)	132(84.1)	0.776
Ambulatory	69(13.2)	46(12.5)	23(14.6)	
Bedridden	8(1.5)	6(1.6)	2(1.3)	
History of Tuberculosis infection				
No	427(81.5)	303(82.6)	124(79.0)	0.334
Yes	97(18.5)	64(17.4)	33(21.0)	
OIs other than Tuberculosis				
No	477(91.0)	327(89.1)	150(95.5)	***0.018***
Yes	47(9.0)	40(10.9)	7(4.5)	
Receipt of TPT				
No	139(26.5)	93(25.3)	46(29.3)	0.314
Yes	385(73.5)	274(74.5)	111(40.7)	
Other known chronic diseases				
No	520(99.2)	364(99.2)	156(99.4)	0.81
Yes	4(0.8)	3(0.8)	1(0.6)	
ART regimens				
ZLE(ZDV + 3TC + EFV)	4(0.8)	4(1.1)	0(0.0)	
TLE(TDF + 3TC + EFV)	361(68.9)	361(98.4)	0(0.0)	
TLN(TDF + 3TC + NVP)	1(0.2)	1(0.3)	0(0.0)	
TLD(TDF + 3TC + DTG)	157(30.0)	0(0.0)	157(100)	
ALE(ABC + 3TC + EFV)	1(0.2)	1(0.3)	0(0.0)	-
Receipt of OPT				
No	139(26.5)	109(29.7)	30(19.1)	***0.012***
Yes	385(73.5)	258(70.3)	127(80.9)	

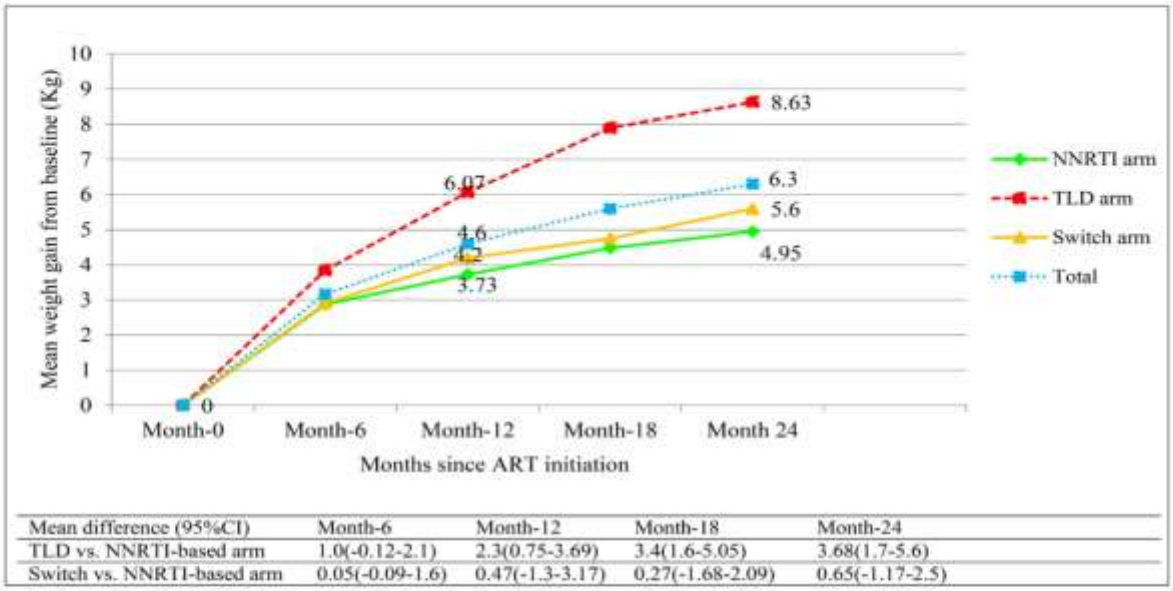
Values presented in number (%) unless otherwise indicated; *, values in median and interquartile range; #, values in means and 95% confidence interval; ABC: Abacavir; CI: confidence interval; DTG: dolutegravir; EFV: efavirenz; 3TC: lamivudine; OIs: opportunistic infections; OPT: opportunistic infections prophylaxis treatment (cotrimoxazole); TPT: Tuberculosis prophylaxis treatment (isoniazid (INH) or isoniazid-rifapentine (3HP)); Kg: kilogram; m: meter; NNRTI-based: non-nucleoside reverse transcriptase inhibitor plus backbone nucleos(t)ide reverse transcriptase inhibitors; TLD: Tenofovir disoproxil fumarate plus lamivudine and dolutegravir; ZDV: zidovudine.

2.08–2.58 kg/m^2) at month 24. Participants who initiated the TLD regimen gained a mean of 3.11 kg/m^2 (95%CI: 2.62–3.60 kg/m^2) compared to 1.84 kg/m^2 (95% CI: 1 .44–2.25 kg/m^2) gain in the NNRTI-based arm at 24 months, ($p<0.0001$) (Figure 1B).

Females who started the TLD regimen gained significantly more weight than females in the NNRTI-based arm (5.8 kg vs. 3.3 kg, $p=0.009$) at 12 months, and (8.6 kg vs. 3.6 kg, $p<0.0001$) at 24 months, respectively (Figure 2A). However, females in the switch arm gained insignificantly greater weight than females in the NNRTI-based arm (Figure 2B). In addition, males who started the TLD regimen gained more weight at 18 months compared to males in the NNRTI-based arm (8.3 kg vs.5.5 kg, $p=0.024$), respectively (Figure 2C). However, weight gain among males in the switch arm was not significantly different from those males in the NNRTI-based arm (Figure 2D). Moreover, the BMI gain also revealed similar trends like body weight (Figure S2).

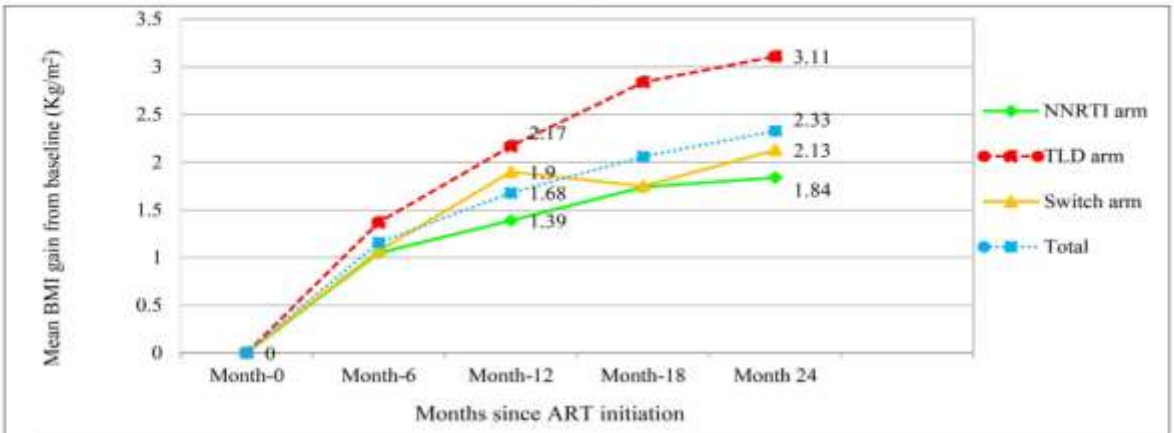
Regarding intra-regimen comparison, only males in the NNRTI-based arm gained significantly greater weight than females in the NNRTI-based arm at month 18 (5.5 kg vs.3.9 kg, $p=0.047$), and at month 24 (7.1 kg vs. 3.6 kg, $p=0.001$).

In the linear mixed-effects model, the mean weight of individuals who started ART with a TLD regimen was 0.23 kg lower than that of those who started ART with an NNRTI-based regimen ($\beta = -0.23$; 95% CI: −2.43–1.96; $p=0.84$). After controlling for time, age, TB co-infection, and gender, the mean weight of the switched arm was 1.82 kg greater than the NNRTI-based arm ($\beta=1.82$; 95% CI: 0.35–3.30; $p=0.015$). Individuals



Mean difference (95%CI)	Month-6	Month-12	Month-18	Month-24
TLD vs. NNRTI-based arm	1.0(-0.12-2.1)	2.3(0.75-3.69)	3.4(1.6-5.05)	3.68(1.7-5.6)
Switch vs. NNRTI-based arm	0.05(-0.09-1.6)	0.47(-1.3-3.17)	0.27(-1.68-2.09)	0.65(-1.17-2.5)

A



Mean difference (95%CI)	Month-6	Month-12	Month-18	Month-24
TLD vs. NNRTI-based arm	0.32(-1.0-0.75)	0.78(0.21-1.3)	1.1(0.47-1.8)	1.27(0.51-2.0)
Switch vs. NNRTI-based arm	0.02(-0.21-1.01)	0.51(-0.34-1.36)	0.01(-0.69-0.77)	0.29(-0.44-1.0)

B

Figure 1. Body weight and BMI increase across treatment arms during ART follow-up (weight increase: A and BMI increase: B).
Abbreviations: BMI: body mass index; Kg: kilogram; m^2: meter square; NNRTI: non-nucleoside reverse transcriptase inhibitor plus backbone nucleos(t)ide reverse transcriptase inhibitors; TLD: Tenofovir disoproxil fumarate plus lamivudine and dolutegravir; (p-value for difference in weight gain between the TLD initiated vs. NNRTI-based arm: 0.001 at month-12; <0.0001 at month-18 and month-24); (p-value for difference in BMI gain between the TLD initiated vs. NNRTI-based arm: 0.003 at month-12; <0.0001 at month-18 and month-24).

infected with TB at the start of ART had a 3.77 kg lower mean weight than those who were not infected with TB (β =-3.77; 95% CI: −6.31 to −1.24; $p=0.004$). In addition, the mean weight of male individuals was 5.75 kg greater than that of female participants (β = 5.75; 95% CI: 3.73–7.77, $p<0.0001$). Time was also found to be a significant predictor of weight gain. The weight increased by 1.44 kg as the treatment time increased by six months (β = 1.44; 95% CI: 1.23–1.66, $p<0.0001$). Statistically significant interaction effects between time and ART regimens have been observed, with treatment starting with a TLD regimen having 0.71 kg higher weight (β = 0.71; 95% CI: 0.34–1.07; $p<0.0001$) and 0.244 kg/m^2 higher BMI (β = 0.244; 95% CI: 0.10–0.39; $p=0.001$) than the NNRTI-based regimens (Table S1).

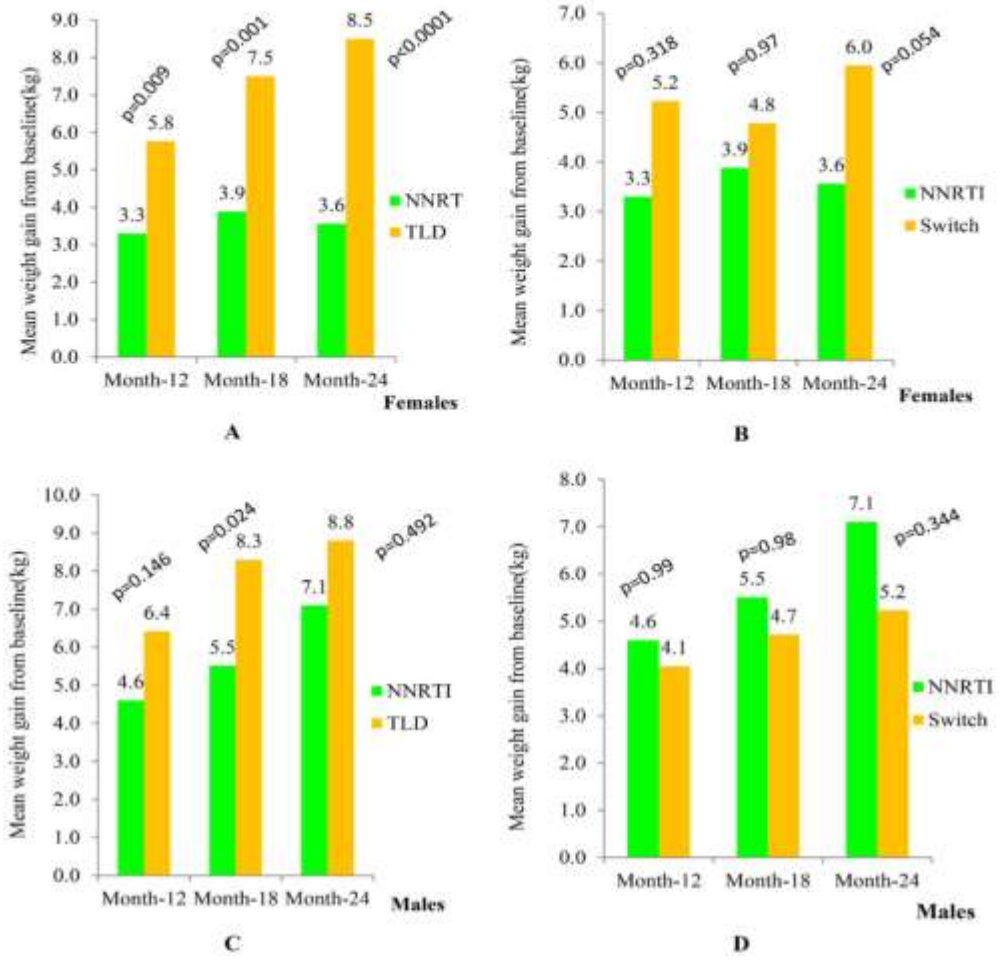


Figure 2. Body weight increase across treatment arms after ART initiation.
Abbreviations: Kg: kilogram; NNRTI: non-nucleoside reverse transcriptase inhibitor plus backbone nucleos(t)ide reverse transcriptase inhibitor; TLD: Tenofovir disoproxil fumarate plus lamivudine and dolutegravir; switch, transitioned from NNRTI-based regimen to TLD.

Incidence of excess weight and BMI gain at 24 months of ART follow up

In total, 262 (50%) of PLWH had gained ≥10% weight after 24 months of ART, of these, 50.2% of them were females. The proportion of PLWH who gained ≥10% weight was 44.1%, 59.2%, and 47.9% for the NNRTI-based arm, TLD arm and the switched arm, respectively. A weight gain ≥10% occurred more frequently in the TLD-initiated arm (59.2%) than in the NNRTI-based arm (44.1%), $p=0.01$ (Table S2). In addition, 40.4%, 61.9%, and 51% of females experienced ≥10% weight gain in the NNRTI-based arm, TLD arm, and the switched arm compared to 50%, 56.2% and 44% of males, respectively.

The rate of participants who gained BMI ≥1kg/m^2 was 66.2% (319/482); of them, 56.4% (180/319) were females (Table S3). About 18.2% of participants became newly overweight to obese (BMI ≥25 kg/m^2), with 11.8% overweight and 6.4% obese. In addition, 17.4% of males became overweight (Figure 3A), while 5.3% of males and 2.2% of females became newly obese (Figure 3B). Treatment-emergent overweight and obesity were greater in the TLD-started arm compared to the NNRTI-based arm (Figure 3C,D). A BMI gain of ≥1kg/m^2 was considerably higher in individuals with a baseline BMI of <25kg/m^2 than those with a baseline BMI of ≥25 kg/m^2 (83.4% vs. 16.6%; $p=0.037$), respectively (Table S4). Moreover, 18.4% and 10.2% of BMI-normal adults who started the TLD regimen became overweight and obese, respectively, compared to 11.8% and 5.3% of those who received the NNRTI-based therapies.

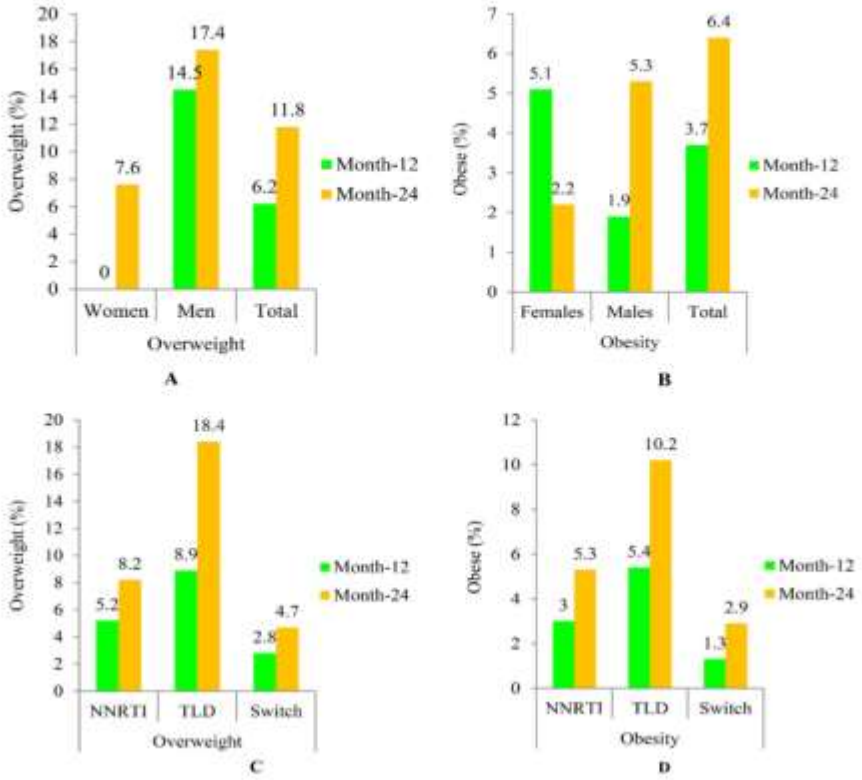


Figure 3. The proportion of newly emerged overweight/obesity after ART initiation (gender-based: A and B; and regimens-based: C and D).
Abbreviations: Overweight (BMI = 25–29.9kg/m²); Obesity(BMI ≥30kg/m²); NNRTI based arm, non-nucleoside reverse transcriptase inhibitor plus backbone nucleos(t)ide reverse transcriptase inhibitors; TLD: Tenofovir disoproxil fumarate plus lamivudine and dolutegravir; switch arm, transitioned from NNRTI-based regimens to TLD.

Factors associated with ≥10% weight gain after 24 months of ART follow up

To determine factors associated with body weight gain, we used ≥10% weight gain as an outcome variable after 24 months of treatment follow-up. Treatment initiation with TLD regimen resulted in higher odds of ≥10% weight gain than treatment initiation with NNRTI-based regimens. Adults who initiated the TLD regimen had 1.9 times greater odds to gain ≥10% of their initial weight than those who started the NNRTI-based regimens (adjusted odds ratio [AOR]: 1.9; 95% CI: 1.19–3.04) (Table 3).

Discussion

The study subjects who initiated ART with the TLD regimen gained significantly more weight and had greater BMI than the NNRTI-based regimens. Compared to NNRTI-based regimens, starting treatment with the TLD regimen was significantly associated with ≥10% weight gain. In addition, older age and other baseline factors such as the WHO disease stages, functional status and body weight were associated with ≥10% weight gain.

In this study, participants who started ART with the TLD regimen gained significantly more weight than those who started the NNRTI-based regimens after 12- and 24 months. This finding is consistent with several clinical trials and observational studies that examined the same problem in other populations, such as a recent 48-week open-label randomized trial in South Africa [20], an 18-month cohort study in South-eastern US [9], a 2 and 5-year cohort study in the Northern US and Canada [9], a meta-analysis of eight clinical trials [10], and a 48-week open-label, multicentre, randomized study in Cameroon [21]. In support, the use of INSTI medications has been associated with more weight gain than PIs or NNRTIs; however, elvitegravir/cobicistat was associated with lesser weight gain than DTG and bictegravir. Among NNRTIs, rilpivirine was

Table 3. Factors associated with ≥10% of weight gain at 24 months after ART initiation.

	Weight gain after ART initiation				
Variable category	Total 524(%)	<10% 262 (%)	≥10% 262 (%)	COR 95%CI	AOR 95%CI
Gender					
Females	297(56.7)	148(56.5)	149(56.9)	1.02(0.72–1.4)	1.06(0.72–1.58)
Male	227(43.3)	114(43.5)	113(43.1)	1.00	1.00
Age					
<40 years old	346(66)	190(72.5)	156(59.5)	1.00	1.00
≥40 years old	178(34)	72(27.5)	106(40.5)	1.79(1.24–2.59)**	2.02(1.35–3.02)**
Baseline body weight					
<50 kg	124(23.7)	35(13.4)	89(34.0)	3.34(2.1–5.2)**	3.0(1.86–4.84)**
≥50 kg	400(76.3)	227(86.6)	173(66.0)	1.00	1.00
ART regimen arms					
NNRTI-based arm	179(34.2)	100(38.2)	79(30.2)	1.00	1.00
TLD arm	157(30.0)	64(24.4)	93(35.5)	1.84(1.19–2.84)**	1.9(1.19–3.04)**
Switch arm	188(35.9)	98(37.4)	90(34.4)	1.16(0.77–1.75)	1.2(0.76–1.88)
History of tuberculosis infection					
No	427(81.5)	232(88.6)	195(74.4)	1.00	1.00
Yes	97(18.5)	30(11.5)	67(25.6)	2.66(1.66–4.25)**	1.36(0.62–2.96)
Baseline WHO clinical stage					
I and II	347(66.2)	204(77.9)	143(54.6)	1.00	1.00
III and IV	177(33.8)	58(22.1)	119(45.4)	2.93(2.0–4.28)**	1.78(1.1–2.86)*
Baseline functional status					
Working	447(85.3)	244(93.1)	203(77.5)	1.00	1.00
Ambulatory and bedridden	77(14.7)	18(6.9)	59(22.5)	3.94(2.25–6.89)**	2.0(1.05–3.8)*
TPT received					
No	138(26.3)	54(20.6)	84(32.1)	1.82(1.22–2.7)**	1.0(0.54–1.9)
Yes	386(73.7)	208(79.4)	178(67.9)	1.00	1.00
OPT received					
No	139(26.5)	88(33.6)	51(19.5)	1.00	1.00
Yes	385(73.5)	174(66.4)	211(80.5)	2.09(1.4–3.12)**	1.35(0.87–2.12)

AOR: adjusted odds ratio; CI: Confidence interval; COR: crude odds ratio; NNRTI-based: non-nucleoside reverse transcriptase inhibitor plus backbone nucleos(t)ide reverse transcriptase inhibitors; OPT: opportunistic infections prophylaxis treatment(cotrimoxazole); TPT: Tuberculosis prophylaxis treatment (isoniazid (INH) or isoniazid-rifapentine (3HP)); TLD: Tenofovir disoproxil fumarate plus lamivudine and dolutegravir; switch, transitioned from NNRTI-based regimen to TLD; WHO: World Health Organization; (overall model fit control statistics for the final model was as follows: (X^2(df = 8) =12.841, $p < 0.001$, -2Log probability = 640.404, Nagalkerke R^2 = 0.202, total percent predicted 67.4%, and Hosmer and Lemeshow's test of significance, $p = 0.117$); *, $p < 0.05$; **, $p < 0.01$.

associated with higher weight gain than efavirenz. Among N(t)RTIs backbone, Tenofovir alafenamide (TAF) is also associated with higher weight gain than TDF, ABC, or ZDV [10]. In addition, weight gain associated with INSTI drugs has also been reported in low- and middle-income countries [21] and also resource-rich settings [10]. The exact mechanism of drug-induced weight gain by INSTIs is unknown, but some clinical studies suggest that INSTIs may impair appetite regulation in the central nervous system (CNS), particularly melanocortin-4 receptor (MC4R), which is a key receptor in the CNS that regulates caloric intake through modulating leptin signaling and is involving in energy homeostasis and appetite regulation [22]. Supportively, studies *in vitro* animal models have shown that MC4R knockout mice suffer from severe obesity [23,24] and the MC4R gene is shared by both mice and humans.

PLWH who initiated treatment with the TLD regimen gained an average BMI of 3.1 kg/m^2, while the switch arm also gained 2.1 kg/m^2 at 24 months of ART follow-up. This may increase the risk of metabolic and cardiovascular disease with long-term treatment in this population. For instance, a study report revealed that a 1 kg/m^2 increase in BMI after starting ART could have a 12% increased risk of developing diabetes and an 18–20% increased risk of developing cardiovascular disease, irrespective of the pre-ART BMI [4]. In addition, the study findings from Veterans Affairs showed that PLWH had a 14% increased risk of developing diabetes mellitus when their weight increased by 5% compared to veterans without HIV infection [5].

Several studies reported a greater weight gain after subjects switched from protease inhibitors (PIs)- or NNRTI-based regimens to INSTIs-based regimens compared to those who received the NNRTI-based regimens; however, the difference was not statistically significant [25–28]. This is consistent with the findings of the present study, which indicate greater weight gain in the switch arm compared to the NNRTI-based arm after 24 months of ART. Contrary to our findings, several studies showed that virologically suppressed people who received the NNRTI-based therapies and then switched to the INSTI-based drugs, particularly a combination of DTG, gained significantly more weight than those who continued the NNRTI-based regimens [10,27,29,30]. Treatment experience with non-INSTI-based regimens before switching, length of time with

INSTIs-based drugs after switching, and practice of switching prior to INSTIs may have contributed to the differences.

In this study, ART initiation with TLD regimen predicted significantly greater weight and BMI gain over time, and ART initiation with TLD resulted in 1.9 times higher odds of ≥10% weight gain than the NNRTI-based regimens. Similarly, a meta-analysis of eight clinical trials conducted by Sax et al. [10] and other observational studies [9,27,31] have shown a significant association between weight gain and INSTI-based regimens in general and the DTG-based regimens in particular, with greater weight gain compared to the NNRTI- or PI-based therapies. The finding of this study indicated that subjects with ambulatory and bedridden functional status had 2.0 times higher odds to gain ≥10% of their initial weight than those with working functional status. This finding is consistent with other studies conducted elsewhere [32–34]. In addition, the present study indicated that people with advanced WHO clinical stages (stages III and IV) during ART initiation had 1.78 times higher odds to gain ≥10% of their initial weight than those with mild clinical stages (stages I and II). The finding is in line with the studies conducted elsewhere [10,35,36], and this may reflect the severity of HIV disease prior to ART initiation and return to health after the start of ART particularly in individuals with more advanced clinical stages. However, other studies have reported similar effects with baseline low CD4+ count [10,31,37,38] and baseline high HIV-1 RNA copies [10,36,39]. The inclusion criteria in our study was targeted at the WHO's test-and-treat strategy [12,13], which focuses only on a positive laboratory diagnosis of HIV result for ART initiation, regardless of CD4+ cells level or the WHO clinical stages of the individuals. Moreover, those individuals who weighed less than 50 kg at baseline and were ≥ 40 years old had 3.0 times and 2.0 times greater odds to gain ≥10% of their initial weight, respectively than their counterparts. Similarly, a study report from Tanzania [40] and other studies showed a significant association between baseline body weight and older age with excess weight gain [39,41]. Large-scale studies also revealed people who were underweight at the baseline of ART and had evidence of more advanced untreated HIV infection gained ≥10% of their body weight during ART follow-up [42].

Moreover, linear mixed-effects model analysis revealed that individuals infected with TB at the start of ART had a 3.77 kg lower mean weight than those who were not infected with TB. Similarly, the study indicated that people with advanced disease stages may have poor weight gain because of OIs, particularly TB, or increased energy expenditure from higher metabolic demands [35].

Furthermore, this study showed a significant difference in weight and BMI increase across treatment groups within female participants, however; females did not show a significant association with ≥10% weight gain compared to males. Consistent with our findings, a recent large multi-cohort study showed a non-significant association between gender and weight gain [43]. In contrast to the present study, previous studies reported an association between weight gain and female sex, particularly among those who initiated treatment with INSTIs-based regimens [10,31,39,41]. This could be attributed to the ethnic effect on weight gain, which contributes to the differences between the studies.

Strengths and limitations of the study

As strengths, this study compared the effects of starting ART with TLD or switching to TLD therapy compared to NNRTI-based regimens on weight and BMI increase and potential predictors of excess weight gain in seven ART-providing healthcare facilities. In addition, we included all adults who started first-line ART after Ethiopia adopted the WHO test-and-treat strategy [12,13]. This test-and-treat strategy only focuses on a positive HIV diagnosis for ART initiation, regardless of the CD4+ count, WHO clinical stage, or other criteria. As a result, this may be useful in limiting the participation of people with a low CD4+ count, advanced disease stages, or wasting syndrome to minimize their confounding effect on weight gaining pattern analysis.

However, this study has certain limitations associated with the design of retrospective studies. As a retrospective investigation, the results might vary from a prospectively conducted cohort study. In addition, we only included participants who had complete data on outcome variables, which could result in ascertainment bias. Confounding factors such as socioeconomic status, calorie intake, physical activity, smoking, and alcohol consumption were absent from participants' medical records but could impact weight gain. In addition, potential factors that can contribute to weight gain such as the onset of diabetes; hypertension, dyslipidemia and use of concomitant medications were not documented in the medical charts in most health facilities and have not been evaluated.

Conclusion

We found that DTG-based therapy (TLD) was associated with greater weight and BMI and also excess

weight gain compared to NNRTI-based therapies after two years of ART initiation. A significant interaction effect was observed between ART regimens and time in predicting weight and BMI gain. In addition, older age and other baseline factors such as the WHO clinical stages, functional status, and body weight were also associated with a weight gain of ≥10%. Irrespective of the improved tolerability and efficacy of INSTI-based ART regimens, post-treatment excess weight gain however needs attention as it may increase the risk of non-HIV/AIDS comorbidities such as metabolic and cardiovascular diseases. Therefore, the cardio-metabolic implications of weight gain after the initiation of DTG-based regimens in this population should be monitored and thoroughly investigated.

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Authors' contributions

ATH hypothesized the study. ATH, ZD, DY and AA designed the study. ATH contributed to data collection and analysis. ATH, ZD, DY and AA drafted the manuscript. ZD, DY and AA supervised data analysis and interpretation, revised the manuscript and gave final approval for the version to be published. All authors read and approved the final manuscript.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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Data availability statement

The data are not publicly available due to privacy or ethical restrictions and is available upon reasonable request to the corresponding author with the authorization of Hawassa city administration, health department office, and ethics committee.

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PAPER II

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The association between dolutegravir-based antiretrovirals and high blood pressure among adults with HIV in southern Ethiopia: a cross-sectional study

Agete Tadewos Hirigo, Daniel Yilma, Ayalew Astatkie and Zelalem Debebe

Abstract

Background: Dolutegravir (DTG), a novel antiretroviral therapy (ART) for HIV, is increasingly adopted across sub-Saharan Africa. However, its impact on blood pressure in Ethiopia remains unclear, highlighting a need for further studies.

Objective: This study aimed to investigate the association between DTG-based first-line regimens and other covariates of high blood pressure (HBP) among adults living with HIV receiving care at health facilities in Hawassa City, southern Ethiopia.

Design: A cross-sectional study.

Methods: Data were collected between January 2023 and May 2024 among 444 systematically selected adults, complemented with a review of their medical records. HBP was defined according to the seventh report of the Joint National Committee (JNC7) guidelines, with a threshold of systolic or diastolic blood pressure of ⩾120/80 mmHg. Multivariable logistic regression analysis was performed to identify predictors of HBP. Adjusted odds ratios (AORs) with 95% confidence intervals (CIs) were computed to determine statistically significant associations.

Results: Of the study participants, 58.3% were women and 41.7% were men, resulting in a response rate of 95.5%. The mean (standard deviation (SD)) age of the participants was 38.4(±8.9) years. The prevalence of HBP was 57.9% (95% CI: 52.5–62.4), with 40.5% classified as prehypertension and 17.3% as hypertension. Among participants with hypertension, 84.4% were newly diagnosed. Initiating ART with DTG-based regimens was associated with higher odds of HBP (AOR 5.9; 95% CI: 1.5–22.7) and switching to DTG-based regimens also increased the odds of HBP (AOR 3.8; 95% CI: 1.1–13.9). Other significant covariates associated with HBP included being male (AOR 2.6; 95% CI: 1.4–4.9), age >45 years (AOR 2.0; 95% CI: 1.2–3.4), high waist-to-height ratio (AOR 2.4; 95% CI: 1.1–4.9), inadequate vegetable intake (AOR 1.7; 95% CI: 1.0–2.7), low physical activity (AOR 2.4; 95% CI: 1.1–5.4), and LDL-cholesterol (AOR 1.1; 95% CI: 1.0–1.2).

Conclusion: Proactive blood pressure screening and management are important for individuals on DTG-based regimens. In addition, early identification and intervention of modifiable risk factors through comprehensive strategies and regular screenings are pivotal for improving cardiovascular health among individuals on ART.

Plain language summary

The association between dolutegravir based antiretroviral therapy and high blood pressure among adults with HIV in southern Ethiopia

This study in southern Ethiopia evaluated blood pressure in adults with HIV on first-line antiretroviral treatment (ART). The rate of high blood pressure (HBP) was 57.9%, with

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40.5% classified as prehypertension and 17.3% as hypertension. Among participants with hypertension, 84.4% were newly diagnosed in this study. ART initiating or switching to DTG-based first-line regimens was significantly associated with HBP compared to efavirenz-based regimens. Additionally, factors such as male sex, advanced age, waist-height ratio, low vegetable intake, inadequate physical activity, and low density lipoprotein cholesterol levels were significantly associated with the prevalence of HBP. Therefore, addressing post-treatment HBP in individuals on DTG based regimens is essential for enhancing cardiovascular health. In addition timely identification and management of modifiable risk factors, supported by comprehensive strategies and routine screenings are vital for this population.

Keywords: antiretroviral therapy, blood pressure, dolutegravir, Ethiopia, HIV, hypertension

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Introduction

The improved accessibility of and adherence to combination antiretroviral treatment (cART) have resulted in a remarkable increase in the life expectancy of people living with HIV (PLWH).[1] However, the increased burden of noncommunicable diseases (NCDs) in this population, particularly in low- and middle-income countries (LMICs), has posed new challenges.[2] NCDs such as cardiovascular diseases (CVDs), diabetes, hypertension (HTN), and certain cancers[2] are becoming increasingly prevalent among PLWH in LMICs.[3,4] Globally, an estimated 1.28 billion adults aged 30–79 have HTN, with two-thirds residing in LMICs. Notably, approximately 46% of adults with HTN are unaware of their condition.[5] This issue is particularly concerning as it affects not only the general population but also PLWH. Compared to individuals without HIV, PLWH are more susceptible to CVD risk factors and experience higher rates of cardiovascular morbidity and mortality.[6] In addition, a significant proportion (35%) of adult PLWH who receive cART globally have HTN.[7]

The rise in HTN is largely attributed to factors such as long-term exposure to cART and underlying inflammation related to HIV infection itself.[3,4] In addition khat (Catha edulis) chewing,[8] age, male sex, obesity, history of alcohol consumption,[9,10] smoking,[11] family history of hypertension and a sedentary lifestyle[12] were risk factors of elevated blood pressure. Studies have also shown an association between anxiety and/or depression[13] and central adiposity[14] with HTN. Moreover, various mechanisms such as adipogenesis and lipodystrophy, activation of the adipocyte, the renin–angiotensin system (RAAS), immune reconstitution, dyslipidemia, chronic systemic and vascular inflammation and renal insufficiency[15] can potentially impact the development of HTN among PLWH.

The adoption of integrase strand transfer inhibitors (INSTIs), especially regimens based on dolutegravir (DTG), has become increasingly preferred as first- and second-line treatment options in LMICs, particularly following approval by the World Health Organization (WHO).[16] This is because the effectiveness and low risk of drug resistance make them ideal for treating HIV. In addition, the safety profile, with fewer interactions and side effects than older medications also enhanced their approval.[16]

Despite their efficacy, DTG-based regimens have been associated with cardiometabolic risks,[17] including a possible association with higher rates of HTN compared to non-nucleoside reverse transcriptase inhibitors (NNRTIs) regimens.[18] The mechanisms behind the association between DTG and weight gain are not fully understood, but increased adipose tissue activation and RAAS modulation may play a role, potentially raising the risk of blood pressure.[19] In addition, studies indicated that individuals starting or switching to

DTG-based regimens often experienced excess weight gain[20,21] and the association between obesity and HTN is well established.[22,23]

DTG-based cART is now widely used across Africa, including in countries like Ethiopia following endorsement by the WHO.[16] However, despite the growing adoption of DTG, there is still a lack of data on its association with NCDs, particularly in East African settings.[10,23] To the best of our knowledge, there is currently no published data on the association between high blood pressure (HBP) and DTG-based regimens, especially in the context of treatment initiation following the implementation of a universal test-and-treat strategy in Ethiopia. Consequently, this study aimed to determine DTG-based first-line regimens and other covariates of HBP among adults living with HIV in southern Ethiopia.

Methods

Study design, setting, and period

This institution-based cross-sectional study was conducted between January 2023 and May 2024, at health facilities in the Hawassa City administration. Hawassa is the capital city of Sidama Regional State and is located approximately 275 km to the south of Addis Ababa, the capital city of Ethiopia. The city administration encompasses 157.2 sq km and is divided into eight subcities and 32 kebeles. According to the 2022 population profile report from the Hawassa City Health Department office, the city administration has a total population of 402,903 with a nearly equal distribution of 201,371 females and 201,532 males.

Population

The study included adult PLWH aged 18–65 years who were receiving cART. Currently, eight health facilities offer ART services in Hawassa City administration for more than 6300 PLWH. However, the study did not include participants from two health facilities based on their personal preferences.

Inclusion and exclusion criteria

The study enrolled individuals who regularly attended the health facilities of the city administration and commenced their CART after Ethiopia adopted the test-and-treat strategy in February 2017. In addition, those who met the following specific criteria were included: they had been on first-line cART for at least 12 months, had HIV ribonucleic acid (HIV-1 RNA) viral load of <1000 copies/mL and demonstrated adequate adherence to cART as per National consolidated guidelines for comprehensive HIV prevention, care, and treatment.[24] Concerning ART regimens, individuals who initially started ART with two nucleos(t)ide reverse transcriptase inhibitors (*N*(*t*)RTIs) and one NNRTI, either remained on this regimen or subsequently switched to DTG-based first-line therapies. In addition, individuals who initiated treatment with a DTG-based first-line regimens and remained on these regimens throughout the study were included in the study. However, participants who had switched to other first line regimens more than once, had severe illnesses or physical disabilities or were pregnant were excluded from the study.

Sample size and sampling techniques

The required sample size for this study was calculated using Centers for Disease control and Prevention (CDC) Epi Info version 7.2 software using a single population proportion formula, assuming a 95% confidence interval (CI), a significance level (α) of 0.05 and a margin of error of 0.05. Using an 18.5% prevalence rate of HTN among PLWH on ART in Ethiopia,[12] an initial sample size of 258 was calculated accounting for a 10% nonresponse rate. Again we determined the sample size using risk factors for HTN at a 95% CI, power of 80 and a 1:1 ratio of unexposed to exposed participants. The HTN prevalence among individuals who were not exposed to DTG-based regimens was 39.1% and exposure to DTG was associated with an increased risk of HTN (adjusted odds ratio (AOR] = 2.4).[25] Considering a 10% nonresponse rate, the sample size was calculated to be 207. However, this study was conducted as part of a larger NCD project with multiple objectives. The sample size of 279 was calculated based on a 23.9% prevalence rate for one of the NCDs,[26] which was larger than the sample size calculated for blood pressure. To maximize representativeness, a total sample size of 279 was accepted for the evaluation of all NCDs including blood pressure. Accounting for a 10% nonresponse rate and a design effect of 1.5, the final sample size was adjusted to 465. A sample size of 465 was then proportionally

allocated to each health facility based on the number of PLWH on first-line ART at each study site. Sampling intervals were determined by dividing the number of PLWH on first-line regimens by the allocated sample size for each facility. Following this, a systematic random sampling technique was then applied to select participants at each facility.

Data collection tools and procedures

The data collection questionnaire was first developed by adapting the WHO stepwise approach[27] and reviewing different literatures. This structured questionnaire covered sociodemographic, economic, anthropometric, lifestyle, and behavioral and clinical variables. The questionnaire was then translated into Amharic by a proficient bilingual language expert. After obtaining signed informed consent, trained nurses administered data collection questionnaires to participants at the ART clinics of the study health facilities. In addition, patients' medical records were reviewed to extract information such as HIV-related factors, ART medications, comorbid conditions, and other relevant data.

Variables and measurement

Variables such as physical measurements that include systolic blood pressure (SBP) and diastolic blood pressure (DBP); and anthropometric measurements such as height, body weight, waist circumference (WC), and hip circumference (HC) were collected from study participants. The data collectors followed the standard techniques to measure each variable. Participants rested comfortably for 10 min before measurement, seated with uncrossed legs and ankles in the isolated data collection room. A digital blood pressure monitor (Heuer, model number: 16-200) was used to measure SBP, DBP, and heart rate. This device has a measurement range of 0–300 mmHg for blood pressure and 30–180 beats per minute for pulse. It also offers a diagnostic accuracy of ±3 mmHg for blood pressure and 5% for pulse rate. Two readings were taken within a 5-min interval and the average of these two was recorded. If the measurements differed by more than 5 mmHg, a third reading was taken and the average of the last two readings was recorded to determine the participants' blood pressure.[28,29]

The primary outcome of this study was HBP (prehypertension and HTN) defined according to the seventh report of the Joint National Committee (JNC7),[30] as Ethiopia has incorporated the JNC7 defintion of blood pressure into the National Clinical and Programmatic Management of Major NCDs Guideline.[31] Based on this, HBP was classified as SBP and/or DBP equal ⩾120/80 mmHg, which includes both pre-hypertension and HTN. HTN was defined as SBP/DBP of ⩾140/90 mmHg, or confirmed by a physician, or the individual was taking antihypertensive medications. Pre-HTN was defined as a SBP of 120–139 mmHg and/or a DBP of 80–89 mmHg.[32] Newly diagnosed HTN refers to participants who had a SBP/DBP of ⩾140/90 mmHg and were unaware of their condition prior to this study.

Participants' height was measured using a Seca stadiometer (SECA GmbH and Co, Germany) to the nearest 0.1 centimeter (cm). Body weight and body mass index (BMI) were assessed with an Omron Body Composition Monitor and Scale (Omron HBF-514C: manufactured for Omron Healthcare Co., Ltd, China), which uses bioelectrical impedance analysis (BIA)[33] and measurements were performed according to the manufacturer's protocol. For the assessment, each participant's age, height (in cm), and sex were input into the device. Participants then stood barefoot on the scale, dressed in light clothing, held the display unit with both hands and kept their arms parallel to the floor. The device measures body weight directly and calculates the BMI based on the entered height value of each participant. Then, the BMI was classified according to the WHO category as underweight (<18.5 kg/m^2), normal (18.5–24.9 kg/m^2), overweight (25–29.9 kg/m^2), or obese (⩾30 kg/m^2).[34]

WC was measured at the level of the umbilicus while the participants were standing and wearing light clothing with measurements taken after exhalation. HC was measured around the widest part of the buttocks. Both the WC and HC measurements were performed using a non-stretchable tape measure following the WHO stepwise approach and recorded to the nearest 0.1 cm. In addition, the waist-to-hip ratio (WHR) and waist-to-height ratio (WHtR) were computed by dividing WC by HC and WC by height, respectively. Abdominal obesity was defined as a WC ⩾ 94 cm for males and ⩾80 cm for females.[35] Moreover, a WHR >0.90 in men and >0.85 in women as well as a WHtR ⩾ 0.5 indicate the presence of abdominal obesity.[35]

Participants' physical activity (PA) was measured using the International Physical Activity Questionnaire Short Form (IPAQ-SF).[36] To calculate the metabolic equivalents of task in minutes per week (METs-min/wk) for each specific activity, the METs value of the activity (3.3 for walking (low intensity); 4.0 for moderate PA; and 8.0 for vigorous PA) was multiplied by the minutes spent engaging in that activity. Finally, PA was classified as low activity (<600 METs-min/week), moderate activity (600 to <3000 METs-min/week), or high activity (≥3000 METs-min/week).[36]

Current alcohol consumption, smoking, and khat use refer to individuals who used each of these at least once in the month preceding the study. Ever alcohol drinking, smoking, and khat use denote respondents who have used each of these substances at any point in their lifetime.[37] The participants' mental health conditions were evaluated using a validated Amharic version of the Hospital Anxiety and Depression Scale (HADS) that includes anxiety and depression, as well as their respective severity categories.[38]

Regarding fruit and vegetable (FAV) consumption, participants were asked about their weekly FAV intake in terms of frequency and portion sizes. The WHO recommends five portions of FAV daily, with each portion weighing 80 g.[39] However, none of the participants in this study met the recommended frequency or portion sizes, and the proportion of those consuming FAV daily was also small. As a result, participants were classified based on the frequency of FAV intake per week rather than the recommended portion sizes.

An overnight fasting blood sample was collected from each participant for lipid profile analysis. The samples were then processed and analyzed following standard operating procedures using the Cobas c 501, a module of the Cobas 6000 analyzer series (Roche Diagnostics GmbH, Sandhofer Strasse 116 D-68305 Mannhein, Germany).

Data quality management

Before actual data collection, the Amharic questionnaire underwent pretesting and improvements were made based on participants' feedback. Nurses working in the ART clinics received training on data collection, variable measurement, and ethical principles. In addition, the precision of the blood pressure and weight scale instruments was checked daily using a mercury sphygmomanometer and standard calibration equipment, respectively. Each participant underwent at least two measurements and the average was considered to ensure accuracy in physical, anthropometric, and body composition assessments. The study information was collected using the same equipment and procedures under daily supervision by the principal investigator.

Data processing and statistical analysis

Categorical variables were summarized using frequency, whereas continuous variables were summarized using means with standard deviations (SDs) or medians with interquartile ranges (IQRs) as appropriate. A skewed continuous variable underwent logarithmic or square root transformation prior to logistic regression analysis. The variation between health facilities was minimal, as indicated by an intraclass correlation coefficient, which was 0.039 and reflecting an insignificant facility-level effect. This finding led us to use a standard logistic regression model for analysis. To identify predictors of HBP, we applied a binary logistic regression model. Independent variables with a p-value <0.2 in bivariable analysis were included in the multivariable analysis. In addition, based on findings from previous literature, factors such as fruit consumption, TB infection, anxiety/depression, time since ART initiation, and treatment regimens were included in the multivariable analysis, regardless of their significance level. Moreover, we assessed the interaction effects between ART regimens and selected variables such as sex, treatment duration, age, PA, and BMI on blood pressure. Multicollinearity was assessed through multiple regression analysis by sequentially removing variables with high variance inflation factor (VIF). Tolerance values >0.1 and VIF of <10 were used as cutoffs to determine the candidate variables for the final model. Furthermore, the Hosmer–Lemeshow test was used to determine the model's goodness of fit, with a p-value > 0.05 indicating a well-fit model. The association between outcome and explanatory variables was determined using AORs with a 95% CI. Finally, variables with a p-value < 0.05 were considered to have a significant association. Data entry and statistical analysis were managed using EpiData 3.1 and IBM SPSS 27.0 (IBM Corp., Armonk, NY, USA), respectively.

Results

Sociodemographic and economic features of the study participants

Among the 465 eligible adult PLWH, 444 participants were enrolled in the study, resulting in a response rate of 95.5%. Table 1 summarizes the sociodemographic and economic characteristics of the study participants. Among the participants, 58.3% were women ($n=259$) and 41.7% were men ($n=185$). The mean (±SD) age of the participants was 38.4 (8.9) years, with the majority (67.8%) falling within the 30–49 years age range. Over 90% of the participants were living in urban areas, half were married, 31.1% had completed primary-level education, 43% were employed, and 41.2% reported their monthly income of ⩽2000 Ethiopian birr (ETB).

Pattern of blood pressure among the study participants

The median (IQR) SBP was 117 (107–128) mmHg with a range of 77–249 mmHg, while the median (IQR) DBP was 77 (70–84) mmHg with a range of 45–148 mmHg. The prevalence of HBP was 57.9% (95% CI: 52.5–62.4). The sex-specific rate of HBP was 68.1% (95% CI: 60.5–74.1) for men and 50.6% (95% CI: 44.4–56.8) for women. The prevalence of pre-hypertension was 40.5% (95% CI: 35.4–45) and HTN was 17.3% (95% CI: 13.7–20.9). Among participants with HTN, 84.4% (65/77) were newly diagnosed in this study and were previously unaware of their condition. In addition, 48% (37/77) were identified as having systolic–diastolic HTN (SDH), and 29.9% (23/77) were diagnosed with isolated diastolic HTN (IDH) (Figure 1). The sex-specific rate of pre-HTN and HTN was 44.9% (95% CI: 37.8–51.9) and 23.2% (95% CI: 17.3–29.2) for men and 37.5% (95% CI: 31.7–43.6) and 13.1 (95% CI: 9.3–17.8) for women, respectively.

Among participants with HTN, 20.8% (16/77) were aged 30–49 years, 44.2% (34/77) were aged 40–49 years, and 45.5% (35/77) were married. The rate of HTN was significantly higher in men (55.8%) compared to women (44.2%) (Table S1). More than 44% of the participants were overweight-obese, 37.6% had a history of khat chewing, 5.2% had comorbid health problems, and 32.7% were sedentary to less active in PA. About 14.5% had a history of smoking and 57.8% reported alcohol consumption, with 38.7% being former drinkers and 19.1% current drinkers (Table S2).

Behavioral, clinical, and nutritional characteristics of the study participants

The median (IQR) time since HIV diagnosis was 4.2 (2.3–6.1) years. All participants received cART following the implementation of the universal test-and-treat strategy in Ethiopia and had been on cART for a mean (±SD) of 3.8 (1.9) years, with nearly half (48.9%) having been on treatment for at least 4 years. Only 12 participants (2.7%) and 14 participants (3.2%) reported consuming fruits and vegetables daily, respectively, regardless of the recommended portion sizes. Over 75% of the participants mentioned economic constraints as the main reason for inadequate intake of FAV, while others described factors such as access limitations, lack of desire, the belief that their intake was sufficient, and discomfort while eating (Table 2).

At the time of ART initiation, the majority of participants (62.4%) were classified as having WHO clinical stages I and II disease. In addition, most participants (85.8%) began ART while in a working functional status. Among them, 106 individuals (23.9%) had a history of tuberculosis (TB) infection, with 57.5% (61/106) diagnosed with pulmonary TB and 42.5% (45/106) with extrapulmonary TB.

Predictors of HBP among the study participants

In the bivariable regression model, several factors were significantly associated with high HBP such as sex, age, BMI, family history of HTN, WC, WHR, WHtR, occupational status, vegetable intake, meat intake, alcohol consumption, physical activity, monthly income level, low density lipoprotein cholesterol, and triglycerides.

After adjustment for potential confounding factors using multivariable logistic regression, ART regimens and the other seven variables were found to be significantly associated with HBP. Initiating ART with DTG-based first-line regimens as well as switching to these regimens were significantly associated with higher odds of HBP compared to NNRTI-based first-line regimens. Adults who initiated and remained on DTG-based first-line ART had 5.9 times higher odds of

Table 1. Sociodemographic and economic characteristics of people with HIV on antiretroviral treatment.

Variables	Category	Overall $n=444$ (%)	Blood pressure status		p Value
			High $n=257$ (%)	Normal $n=187$ (%)	
Sex	Female	259 (58.3)	131 (51)	128 (31.6)	<0.001
	Male	185 (41.7)	126 (49)	59 (31.9)	
Age, years	Mean (±SD)	38.4 (8.9)	42.9 (9.9)	38.4 (8.8)	<0.001*
	20–29	51 (11.5)	24 (9.3)	27 (14.4)	<0.001
	30–39	153 (34.5)	70 (27.2)	83 (44.4)	
	40–49	148 (33.3)	96 (37.4)	52 (27.8)	
	⩾50	92 (20.7)	67 (26.1)	25 (13.4)	
Residence	Rural	41 (9.2)	22 (8.6)	19 (10.2)	0.565
	Urban	403 (90.8)	235 (91.4)	168 (89.8)	
Marital status	Single	47 (10.6)	27 (10.5)	20 (10.7)	0.99
	Married	222 (50.0)	129 (50.2)	93 (49.7)	
	Divorced	102 (23.0)	59 (23)	43 (23)	
	Widow/widower	73 (16.4)	42 (16.3)	31 (16.6)	
Education	Unable to read and write	50 (11.3)	27 (10.5)	23 (12.3)	0.727
	Informal	1 (0.2)	1 (0.4)	0 (0.0)	
	Primary level	138 (31.1)	76 (29.6)	62 (33.2)	
	Secondary level	132 (29.9)	78 (30.4)	54 (28.9)	
	At least college	123 (27.7)	75 (29.2)	48 (25.7)	
Occupation	Students	8 (1.8)	5 (1.9)	3 (1.6)	0.005
	Employed	191 (43.0)	120 (46.7)	71 (38)	
	Merchants	89 (20.0)	58 (22.6)	31 (16.6)	
	No job	35 (7.9)	19 (7.4)	16 (8.6)	
	Daily laborers	51 (11.5)	17 (6.6)	34 (18.2)	
	Housewife	48 (10.8)	25 (9.7)	23 (12.3)	
	Farmers	10 (2.3)	4 (1.6)	6 (3.2)	
	Retired and others	12 (2.7)	9 (3.5)	3 (1.6)	
Income in ETB	⩽2000 birr	183 (41.2)	87 (33.9)	96 (51.3)	<0.001
	2001–4000 birr	89 (20.0)	52 (20.2)	37 (19.8)	
	4001–6000 birr	78 (17.6)	51 (19.8)	27 (14.4)	
	6000+ birr	94 (21.2)	67 (26.1)	27 (14.4)	

ETB, Ethiopian birr (1 Ethiopian birr = 0.0173 USD during the study); SD, standard deviation; significance level (by chi-square test; *, by independent *t*-test).

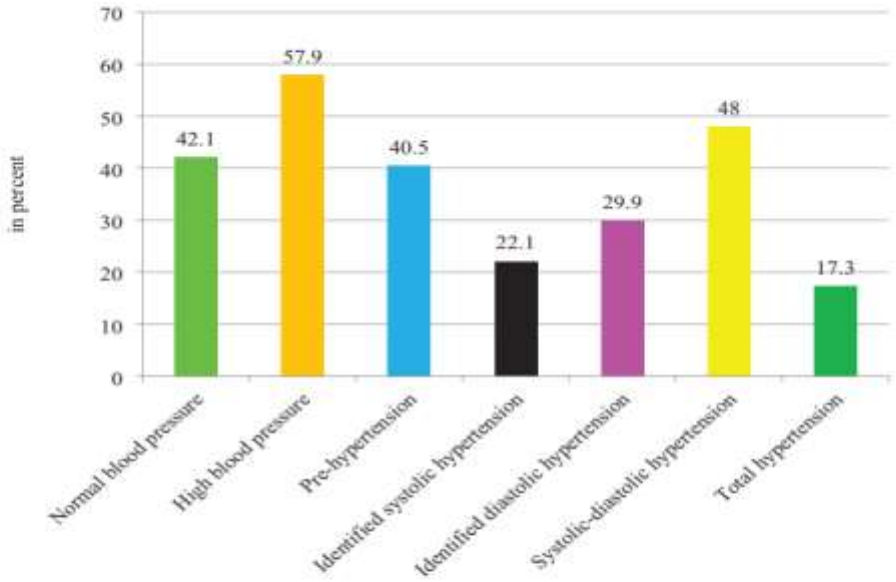


Figure 1. The pattern of blood pressure among the study participants.

developing HBP compared to those on NNRTI-based regimens (AOR: 5.9; 95% CI: 1.5–22.7). While those who switched from NNRTI-based regimens to DTG-based regimens had 3.8 times higher odds of developing HBP compared to those who remained on NNRTI-based regimens (AOR: 3.8; 95% CI: 1.1–13.9). Men had 2.6 times greater odds of developing HBP compared to women (AOR: 2.6; 95% CI: 1.4–4.9). In addition, participants who were older than 45 years had twofold higher odds of developing HBP compared to their younger counterparts (AOR: 2.0; 95% CI: 1.2–3.4). Moreover, participants who consumed vegetables for less than 4 days a week had nearly twofold greater odds of developing HBP compared to those who consumed at least 4 days a week (AOR: 1.7; 95% CI: 1.01–2.7) (Table 3).

Statistically significant interaction effects were found between treatment regimens and independent variables such as male sex, adequate physical activity, and BMI in the prediction of HBP and HTN (Table 4). Sex-stratified analysis indicated that switching to DTG-based regimens, being over 45 years, and having a BMI $\geq 25\,kg/m^2$ were significantly influenced blood pressure with remarkably significant effects observed in women (Table S3).

Discussion

In this study, 57.9% of participants had HBP, with 40.5% classified as pre-hypertensive and 17.3% as hypertensive. Among the 17.3% of participants with HTN, 84.4% (14.6% of the total participants) were newly diagnosed during this study. In addition, initiating treatment with or switching to DTG-based first-line regimens had higher odds of HBP compared to efavirenz-based first-line regimens. Non-modifiable risk factors such as older age and male sex were associated with higher odds of HBP. In addition, inadequate vegetable intake along with other modifiable risk factors such HC, WHtR, lipid profiles, and inadequate PA were also associated with increased odds of HBP.

More than 96% of participants were on DTG-based first-line regimens, either initiated directly or switched from NNRTI-based therapy and 57.9% of participants had HBP in this study. This result is consistent with a study from Ghana, which reported a prevalence of HBP of 54.6%.[40]

Table 2. Behavioral, clinical, and nutritional characteristics of the study participants.

Variables		Category	Total ($n = 444$)	Blood pressure status	
				High $n = 257$ (%)	Normal $n = 187$ (%)
Body mass index, kg/m²		Mean (standard deviation)	24.8 (4.8)	26 (4.7)	23.1 (4.5)
Underweight		≤18.4 kg/m²	27 (6.1)	8 (3.1)	19 (10.2)
Normal weight		18.5–24.9 kg/m²	220 (49.5)	105 (40.9)	115 (61.5)
Overweight		25–29.9 kg/m²	138 (31.1)	100 (38.9)	38 (20.3)
Obese		≥30 kg/m²	59 (13.3)	44 (17.1)	15 (8)
Duration of HIV, years		Median (interquartile range)	4.2 (2.3–6.1)	4.0 (2.4–6.0)	4.3 (2.3–6.2)
Duration on antiretrovirals, years		Mean (standard deviation)	3.8 (1.9)	3.8 (1.8)	3.9 (1.9)
Treatment	AZT/TDF+3TC+EFV	Maintained	17 (3.8)	8 (3.1)	9 (4.8)
regimens	TDF/ABC+3TC+DTG	Switched	205 (46.2)	118 (45.9)	87 (46.5)
	TDF/ABC+3TC+DTG	Maintained	222 (50.0)	131 (51)	91 (48.7)
Smoking		Never smoked	380 (85.6)	222 (86.4)	158 (84.5)
		Former	54 (12.2)	30 (11.7)	24 (12.8)
		Current	10 (2.3)	5 (1.9)	5 (2.7)
Alcohol intake		Never	187 (42.1)	93 (36.2)	94 (50.3)
		Former	172 (38.7)	105 (40.9)	67 (35.8)
		Current	85 (19.1)	59 (23)	26 (13.9)
Comorbidity state		No	421 (94.8)	240 (93.4)	181 (96.8)
		Yes	23 (5.2)	17 (6.6)	6 (3.2)
Fruit intake/week		≤2 days	322 (72.5)	187 (72.8)	135 (72.2)
		3–4 days	89 (20.0)	55 (21.4)	34 (18.2)
		≥5 days	33 (7.4)	15 (5.8)	18 (9.6)
Vegetables intake/week		≤2 days	197 (44.4)	119 (46.3)	78 (41.7)
		3–4 days	160 (36.0)	90 (35)	70 (37.4)
		≥5 days	87 (19.6)	48 (48)	39 (20.9)
Physical activity		≤Less active	145 (32.7)	107 (41.6)	38 (20.3)
		Moderate	243 (54.)	131 (51)	112 (59.9)
		Highly active	56 (12.6)	19 (7.4)	37 (19.8)

(Continued)

Table 2. (Continued)

Variables	Category	Total ($n=444$)	Blood pressure status	
			High $n=257$ (%)	Normal $n=187$ (%)
Intake of meat	≤3 days/month	296 (66.7)	164 (63.8)	132 (70.6)
	1–3 days/week	124 (27.9)	75 (29.2)	49 (26.2)
	≥4 days/week	24 (5.4)	18 (7)	6 (3.2)
Family history of hypertension	No/don't know	294 (66.2)	160 (62.3)	134 (71.7)
	Yes	150 (33.8)	97 (37.7)	53 (28.3)
Waist circumference, centimeter	Median (interquartile range)	85 (76–94)	90 (81–98)	78 (72–88)
Hip circumference, centimeter	Median (interquartile range)	95 (89–102)	98 (91–103)	91 (85–100)
Waist-to-hip ratio	Median (interquartile range)	0.9 (0.83–0.96)	0.92 (0.86–0.98)	0.87 (0.81–0.92)
Waist-to-height ratio	Median (interquartile range)	0.52 (0.47–0.6)	0.54 (0.5–0.6)	0.48 (0.44–0.54)
Triglycerides, milligram/deciliter	Median (interquartile range)	119 (87.9–102)	131 (95–197)	105 (81.9–150)
High density lipoprotein cholesterol, milligram/deciliter	Mean (standard deviation)	36.7 (9.6)	36.8 (9.8)	36.5 (9.4)
Low density lipoprotein cholesterol, milligram/deciliter	Mean (standard deviation)	91 (30.9)	96.1 (31.9)	84 (28.2)
Waist to sitting height ratio	Median (interquartile range)	1.07 (0.96–1.2)	1.1 (1.0–1.2)	0.99 (0.91–1.1)

ABC, abacavir; AZT, zidovudine; DTG, dolutegravir; EFV, efavirenz; 3TC, lamivudine; TDF, tenofovir disoproxil fumarate.

Table 3. Factors associated with high blood pressure among the study participants.

Variables	Category	Total 444 (%)	Blood pressure status		COR (95% CI)	AOR (95% CI)
			High 257 (%)	Normal 187 (%)		
Sex	Male	185 (41.7)	126 (49)	59 (31.6)	2.1 (1.4–3.1)***	2.6 (1.4–4.9)**
Age	>45 years	156 (35.1)	113 (44)	43 (23)	2.6 (1.7–4.0)***	2.0 (1.2–3.4)**
Duration on antiretrovirals	≥6 years	83 (18.7)	48 (18.7)	35 (18.7)	1.0 (0.61–1.6)	1.1 (0.56–2.1)
Body mass index	≥25 kg/m^2	197 (44.4)	144 (56)	53 (28.3)	3.2 (2.1–4.8)***	0.95 (0.48–2.0)
Family history of hypertension	Yes	150 (33.8)	97 (37.7)	53 (28.3)	1.5 (1.02–2.3)*	1.2 (0.75–2.0)
High waist circumference	Yes	131 (29.5)	94 (36.6)	37 (19.8)	2.3 (1.5–3.6)***	0.93 (0.46–1.9)

(Continued)

Table 3. (Continued)

Variables	Category	Total 444 (%)	Blood pressure status		COR (95% CI)	AOR (95% CI)
			High 257 (%)	Normal 187 (%)		
High waist-to-hip ratio	Yes	270 (60.8)	179 (69.6)	91 (48.7)	2.4 (1.6–3.6)***	1.1 (0.58–2.1)
High waist-to-height ratio	Yes	287 (64.6)	200 (77.8)	87 (46.5)	4.0 (2.7–6.1)***	2.4 (1.1–4.9)*
Occupation	Working	280 (63.1)	178 (69.3)	102 (54.5)	1.9 (1.3–2.8)**	1.2 (0.69–2.0)
Fruits intake	≤2 days/week	223 (50.2)	123 (47.9)	100 (53.5)	0.8 (0.55–1.2)	1.0 (0.62–1.7)
Vegetables intake	<4 days/week	302 (68)	185 (72)	117 (62.6)	1.5 (1.02–2.3)*	1.7 (1.01–2.7)*
Tuberculosis infection	Yes	106 (23.9)	66 (25.7)	40 (21.4)	1.3 (0.81–2.0)	1.2 (0.68–2.3)
Intake of meat	≥2 days/week	163 (36.7)	115 (44.7)	48 (25.7)	2.3 (1.6–3.5)***	1.4 (0.81–2.3)
Alcohol use	Ever consumed	257 (57.9)	164 (63.8)	93 (47.9)	1.8 (1.2–2.6)**	0.89 (0.53–1.5)
World Health Organization	stage-II	88 (19.8)	57 (22.2)	31 (16.6)	1.6 (0.97–2.7)	1.7 (0.90–3.2)
Clinical stage	stage-III	118 (26.6)	70 (27.2)	48 (25.7)	1.3 (0.81–2.1)	0.99 (0.54–1.8)
	stage-IV	49 (11.0)	30 (11.7)	19 (10.2)	1.4 (0.74–2.7)	0.94 (0.40–2.2)
Physical activity	≤Less active	145 (32.7)	107 (41.6)	38 (20.3)	4.5 (2.8–10.7)***	2.4 (1.1–5.4)*
	Moderate	243 (54.7)	131 (51)	112 (59.9)	2.3 (1.2–4.2)***	1.6 (0.8–3.3)
Comorbidity	Yes	23 (5.2)	17 (6.6)	6 (3.2)	2.1 (0.83–5.5)	1.5 (0.49–4.7)
Treatment switched to TDF/ ABC + 3TC + DTG		205 (46.2)	118 (45.9)	87 (46.5)	1.5 (0.57–4.1)	3.8 (1.1–13.9)*
Regimens maintained on TDF/ ABC + 3TC + DTG		222 (50)	131 (51)	91 (48.7)	1.6 (0.6–4.3)	5.9 (1.5–22.7)*
Monthly income	≥3500 ETB	198 (44.6)	135 (52.5)	63 (33.7)	2.2 (1.5–3.2)***	0.93 (0.52–1.6)
Anxiety/depression	Yes	18 (4.1)	9 (3.5)	9 (4.8)	0.72 (0.28–1.8)	0.92 (0.30–2.8)
Hip circumference (SqrtT), mg/dl	Mean (SD)	9.7 (0.53)	9.9 (0.49)	9.6 (0.54)	2.9 (1.9–4.3)***	2.4 (1.2–4.8)*
Triglycerides (LogT), mg/dl	Mean (SD)	2.1 (0.22)	2.1 (0.23)	2 (0.2)	7.1 (2.8–17.7)***	2.1 (0.69–6.7)
Low density lipoprotein cholesterol, mg/dl	Mean (SD)	91 (30.9)	96 (31.9)	84 (28.2)	1.01 (1.01–1.02)***	1.1 (1.0–1.02)*

ABC, abacavir; AOR, adjusted odds ratio; COR, crude odds ratio; CI, confidence interval; DTG, dolutegravir; ETB, Ethiopian birr (1ETB = 0.0173USD during the study); EFV, efavirenz; 3TC, lamivudine; LogT, log10 transformed; SD, standard deviation; Sqrt, square root transformed; TDF, tenofovir disoproxil fumarate; Reference category: female-sex; age ≤45 years; ART duration <6 years; BMI < 25 kg/m^2; family history of HTN no; WC normal; WHR normal; WHtR normal; occupation-currently not working; fruit use ≥2 days/week; vegetable use ≥4 days/week; tuberculosis no; meat use<2 days/week; alcohol use-never; smoking-never; WHO clinical stage I; exercise moderate-high; comorbidity no; ART regimen arm: EFV-based; monthly income <3500 ETB; anxiety/depression no; (significance level:*$p < 0.05$; **$p < 0.01$; ***$p < 0.001$).

Table 4. The interaction effect between antiretroviral regimens and other covariates on blood pressure using a multivariable logistic regression model.

Interaction and variables	Treatment category	High blood pressure		Hypertension	
		AOR (95% CI)	*p* Value	AOR (95% CI)	*p* Value
ART regimens × sex	Efavirenz based	Reference		Reference	
	Switched to dolutegravir	2.1 (1.1–4.2)	0.028	2.8 (1.3–6.0)	0.008
	Maintained on dolutegravir	2.0 (1.1–3.5)	0.017	1.2 (0.59–2.5)	0.582
ART regimens × treatment duration, years	Efavirenz based	Reference		Reference	
	Switched to dolutegravir	0.67 (0.52–0.87)	0.002	0.75 (0.55–1.02)	0.70
	Maintained on dolutegravir	0.84 (0.65–1.1)	0.217	1.3 (0.9–1.8)	0.182
ART regimens × age >45 years	Efavirenz based	Reference		Reference	
	Switched to dolutegravir	2.6 (1.3–5.0)	0.007	2.1 (0.98–4.6)	0.056
	Maintained on dolutegravir	1.8 (0.95–3.6)	0.072	0.99 (0.45–2.2)	0.977
ART regimens × low Physical activity	Efavirenz based	Reference		Reference	
	Switched to dolutegravir	2.0 (0.998–5.0)	0.051	0.66 (0.30–1.5)	0.322
	Maintained on dolutegravir	2.3 (1.1–4.6)	0.017	2.3 (1.04–5.0)	0.039
ART regimens × body mass Index, kg/m²	Efavirenz based	Reference		Reference	
	Switched to dolutegravir	1.1 (1.06–1.2)	<0.001	1.1 (1.03–1.16)	0.006
	Maintained on dolutegravir	1.06 (1.01–1.1)	0.008	1.01 (0.95–1.06)	0.787

AOR, adjusted odds ratio; ART, antiretroviral therapy; COR, crude odds ratio; CI, confidence interval; Reference category: female sex, age ≤45 years, moderate to high physical activity.

In addition, a longitudinal study from Zimbabwe reported a significant increase in blood pressure among PLWH on DTG-based regimens over 2 years, while the rate remained stable for those using NNRTIs and protease inhibitors (PIs).[41] However, the findings of the present study were remarkably higher than the 35% prevalence of HBP reported in Zambia.[42] The differences in blood pressure rates within this population may be factors such as genetic diversity, variations in data collection methods (e.g., the use of national electronic records in Zambia versus direct participant contact in our study), treatment initiation criteria, and differences in participant selection criteria.

The prevalence of HTN in this study was 17.3%, which is consistent with several other studies conducted in African settings such as 17.4% in Burundi,[43] 17.4% in Ghana,[44] 14.7% in Zamia,[42] 18.5% in south Ethiopia,[12] 14.2% in South Africa,[21] and 18.4% in Zambia.[25] However, the rate observed in this study was lower than the rates reported in several other studies such as 24.7% in Rwanda,[45] 27.2% in Uganda,[10] and 23% in Europe and Australia.[18] Variations in HTN prevalence across these studies may be attributed to differences in HIV clinical stages at treatment initiation, the effects of different ART regimens on cardiovascular health, ethnic factors, and geographic factors.

Over 44% of participants in this study had a BMI of $\geq 25\,kg/m^2$ and 73.1% of those individuals had HBP, representing 56% of all HBP cases. Similar studies have reported high rates of HTN among individuals who have a BMI $\geq 25\,kg/m^2$.[10,42] The exact mechanisms behind weight gain associated with DTG remain unclear; however, weight gain may increase blood pressure through pathways involving adipose tissue activation and the RAAS system.[19]

In this study, both treatment initiation with DTG-based first-line regimens and switching to these regimens were significantly associated with HBP compared to NNRTI-based regimens. These findings are consistent with prior studies showing a significant association between increased blood pressure and INSTI-based regimens, particularly those containing DTG, leading to a higher rate of elevated blood pressure compared to NNRTI or PI-based regimens.[10,21,41] This may be influenced by the fact that individuals who initiated or switched to DTG-based regimens experienced greater weight gain[20,21,41], which could contribute to increased blood pressure compared to those on NNRTI-based regimens.[21,41] In addition, efavirenz is associated with reduced body weight, which could explain the people taking efavirenz based regimens tend to have lower blood pressure compared to those taking DTG based regimens.[41] The mechanism of DTG's ability to bind and chelate magnesium (Mg^{2+})[46,47] may interfere with magnesium's regulatory role in blood pressure, extending beyond its primary role in integrase inhibition.

The NEAT022 trial found no difference in HTN rates after 48 weeks between individuals who switched from boosted PI-based to DTG-based regimens compared to those who remained on PI-based regimens, in contrast to our findings.[48] A study has reported a strong association between PIs and the pathophysiology of HTN through mechanisms such as RAAS activation, endothelial dysfunction, arterial stiffness, lipodystrophy, insulin resistance, and oxidative stress.[49] This supports the notion that DTG-based regimens may not show significant variability in HTN outcomes compared to PI-based regimens, as both have been found to potentiate increased blood pressure. The observed differences in blood pressure in these studies may reflect variability between study groups, as our participants switched from NNRTI-based to DTG-based regimens, compared to those who remained on NNRTI-based regimens. Another factor that may be attributed to the difference is that participants in the NEAT022 study were on DTG for only 48 weeks after switching, while our participants had been on DTG for a mean duration of 38 months (ranging from 12 to 60 months).

Men showed a higher rate of elevated blood pressure compared to women in this study, indicating significantly greater odds of developing HBP.[9,10,23] Various factors such as hormones and RAAS activation are suggested to contribute to sex-related disparities in blood pressure levels.[50] In support, estrogen, the primary female sex hormone, has been implicated in protecting females from HTN by exerting cardiovascular effects such as vasodilation, anti-inflammatory actions, and modulation of the RAAS, which contribute to blood pressure regulation.[51]

The proportion of HBP and HTN varied significantly with age in this study, with those over 45 years old showing significantly higher odds of HBP compared to their younger counterparts. This finding aligns with previous studies that indicated the association between advanced age and increased blood pressure.[9,10,12,42] Physiological factors such as changes in blood flow, arterial stiffness, neurohormonal imbalances, autonomic system changes, and age-related effects on kidney function possibly contribute to the association between age and HTN among older individuals.[52] Furthermore, the aging process may lead to various structural and functional changes in the arterial vasculature, contributing to the development of HTN and other cardiovascular conditions.[53]

A significant association between PA and blood pressure was observed in the present study, revealing that individuals who engaged in low PA had notably higher odds of developing HBP compared to those who maintained moderate to high levels of PA. This aligns with other studies conducted in Ethiopia.[12,54] In addition, PA contributes to maintaining a healthy weight, improving endothelial function for better blood flow regulation, reducing sympathetic nervous system activity, enhancing insulin sensitivity, and mitigating inflammation and oxidative stress, which are all central factors in lowering blood pressure and promoting cardiovascular health.[55]

Several studies have shown a strong association between HTN and factors such as increased weight.[10,12,44] By contrast, our study found no association between BMI and HBP; however, a significant interaction effect between switching to DTG-based first-line regimens and BMI was observed in predicting increased odds of HBP and HTN in this study. This aligns with previous studies that indicated increased blood pressure among those who switched to DTG was associated with weight gain.[21,22,41,56] Furthermore, we found a significant association between HBP and factors such as lipid profile, low vegetable intake, and high WHtR. The findings are consistent with previous studies highlighting the association between elevated blood pressure and inadequate vegetable intake,[57] lipid profiles,[44] and high WHtR.[58]

This study has several limitations. As a cross-sectional study, it is limited in its ability to establish causality and can only identify associations. The high odds ratio of HBP associated with DTG-based regimens may reflect systematic differences in participant characteristics between the comparison groups. In addition, the limited representation of individuals on efavirenz-based regimens (the reference group), due to the national rollout of DTG-based regimens, may introduce socioeconomic or clinical factors that influence blood pressure. Furthermore, the use of single-phase blood pressure measurements may not capture the dynamic variability of blood pressure throughout the day or in different environments.

Conclusion

The prevalence of HBP among adult PLWH is alarmingly high. HBP was significantly associated with DTG-based first-line regimens compared to NNRTI-based regimens. In addition, a significant interaction effect was observed between treatment regimens and several covariates in predicting increased blood pressure. The study also identified associations between elevated blood pressure and both non-modifiable and modifiable risk factors.

Therefore, proactive blood pressure screening and management are crucial for individuals on DTG based regimens, especially considering the increasing trends in post-treatment blood pressure. In addition, identifying and addressing modifiable risk factors early through comprehensive strategies and regular screenings are also key steps for enhancing cardiovascular health in this population.

Declarations

Ethics approval and consent to participate

The study was approved by the Institutional Review Board (IRB) of the College of Natural and Computational Sciences (CNS-IRB) at Addis Ababa University on September 19, 2022 with reference of IRB/07/14/2022. Before initiating the study, a support letter from the Hawassa City Administration Health Department was obtained and submitted to each study health facility. Permission was also secured from the medical director's office or the head of each health facility. Participants were informed on the study's objectives, potential effects, and the significance of the data collected. Written informed consent was obtained from all participants, as well as from legally authorized representatives for participants unable to read or write, prior to the study's commencement. Participation was entirely voluntary, and participants were made aware of their right to withdraw or decline at any stage. To ensure confidentiality, all information remained anonymous.

Consent for publication

Not applicable.

Author contributions

Agete Tadewos Hirigo: Conceptualization; Data curation; Formal analysis; Funding acquisition; Investigation; Methodology; Project administration; Resources; Software; Writing – original draft; Writing – review & editing.

Daniel Yilma: Conceptualization; Data curation; Formal analysis; Investigation; Methodology;

Software; Supervision; Validation; Visualization; Writing – original draft; Writing – review & editing.

Ayalew Astatkie: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Software; Supervision; Validation; Visualization; Writing – original draft; Writing – review & editing.

Zelalem Debebe: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Supervision; Validation; Visualization; Writing – original draft; Writing – review & editing.

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Competing interests

The authors declare that there is no conflict of interest.

Availability of data and materials

The data are not publicly accessible and it can be accessible with reasonable request from the corresponding author.

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Supplemental material

Supplemental material for this article is available online.

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RESEARCH ARTICLE OPEN ACCESS

Hyperglycaemia and Its Risk Factors Among Adults Living With HIV on Follow-Up at the Hawassa City Administration, Southern Ethiopia: A Cross-Sectional Study

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ABSTRACT

Background: Ethiopia implemented the universal test and treat in 2017 and later adopted dolutegravir-based regimens for people living with HIV (PLWH). However, the impact of these changes on glucose metabolism in Ethiopia remains unclear, highlighting the need for further investigation.

Methods: A cross-sectional study was conducted in southern Ethiopia from 5 January 2023 to 30 May 2024. We included 443 adult PLWH using systematic random sampling. American Diabetes Association criteria was used to define hyperglycaemia. To identify factors associated with hyperglycaemia, binary logistic regression was used with adjusted odds ratio (AOR) and 95% confidence interval (CI).

Results: Overall prevalence of hyperglycaemia was 24.4% (16.7% prediabetes and 7.7% diabetes mellitus [DM]). Of the participants with DM, 82.3% were newly diagnosed. Significant predictors of hyperglycaemia were age > 50 years (AOR 2.1; 95% CI 1.1–3.9), alcohol intake (AOR 2.1; 95% CI 1.02–4.2), obesity (AOR 3.2; 95% CI 1.3–7.9), high waist–hip ratio (AOR 2.6; 95% CI 1.4–5.05) and LDL-cholesterol (AOR 2.2; 95% CI 1.02–4.6). While significant predictors of DM were alcohol intake (AOR 3.0; 95% CI 1.1–8.4), co-morbidity (AOR 2.6; 95% CI 1.1–6.05), high waist circumference (AOR 7.5; 95% CI 1.3–43.3), high waist–hip ratio (AOR 4.1; 95% CI 1.02–16.2) and high triglycerides (AOR 3.2; 95% CI 1.3–7.7). Dolutegravir-based regimen was not associated with hyperglycaemia.

Conclusion: Hyperglycaemia prevalence among adult PLWH on antiretroviral therapy in southern Ethiopia is rising, with most diabetes cases newly identified. This emphasises the critical need for routine screening to enable early detection, prevention and management.

1 | Introduction

Advancements in combination antiretroviral therapy (ART) have transformed HIV into a manageable chronic condition, significantly increasing the life expectancy of adult people living with HIV (PLWH) [1]. However, the rise in life expectancy has been accompanied by an increasing burden of morbidity and mortality from chronic non-communicable diseases (NCDs), particularly in low- and middle-income countries (LMICs) [2].

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The global prevalence of type 2 diabetes mellitus (T2DM) is projected to reach 11.3% by 2030 and 12.2% by 2040 [3]. In 2021, 464 million adults (9.1%) had impaired glucose tolerance (IGT), and 298 million (5.8%) had impaired fasting glucose (IFG) worldwide [4]. In Africa, a systematic review showed a diabetes prevalence of 5.1% and a prediabetes prevalence of 15.2% in adult PLWH [5]. In sub-Saharan Africa (SSA), a systematic review conducted between 2000 and 2021 among PLWH reported a prediabetes prevalence of 13.7% (95% confidence interval [CI]: 10.21–17.59) and a diabetes prevalence of 4.8% (95% CI: 4.02–5.59) [5, 6]. In addition, recent cross-sectional studies have shown a higher prevalence of hyperglycaemia, ranging from 12.8% to 20% [7–10], with 10.3%–10.9% classified as prediabetes and 2.5%–6.3% as diabetes among PLWH receiving dolutegravir (DTG)-based first-line regimens [7, 8]. However, compared to DTG-based regimens, the prevalence of hyperglycaemia was lower among those who received non-nucleoside reverse transcriptase inhibitor (NNRTI)-based regimens, which was 9.4% (with 6.3% prediabetes and 3.1% diabetes) [7].

Older classes of ART drugs, such as protease inhibitors (PIs) and NNRTIs, were used for HIV treatment. However, PIs are associated with metabolic disturbances, including dyslipidemia and insulin resistance, which increase the risk of developing T2DM [11]. Similarly, certain NNRTIs have been implicated in metabolic complications, though to a lesser extent than PIs do [11]. In addition to ART medication effects [12, 13], several other factors contribute to the increased prevalence of hyperglycaemia among PLWH. These include advanced age [12, 14], central obesity [13], hypertension [12, 13], chronic inflammation associated with HIV [15], excessive weight or obesity [16], dyslipidaemia [12, 16] and pulmonary tuberculosis (TB), all of which are associated with insulin resistance [17]. Additional risk factors for hyperglycaemia are certain ethnic backgrounds, a family history of diabetes and male sex [8].

The introduction of newer ART agents, such as integrase strand transfer inhibitors (INSTIs), marked a significant advancement in HIV treatment. Among these, DTG is particularly notable due to its strong antiviral efficacy, high barrier to resistance and better tolerability compared to older drug classes like NNRTIs [18]. In Ethiopia, DTG-based regimens have been included in HIV treatment protocols since 2018 [19], aligning with WHO guidelines intended to optimise treatment efficacy and improve outcomes for PLWH [18].

Despite its therapeutic advantages, DTG has been associated with potential metabolic side effects including obesity, altered glucose metabolism and insulin resistance [8]. However, the literature on the incidence of hyperglycaemia associated with DTG-based regimens reveals inconsistent findings. Some studies suggest a potential association between the use of DTG-based regimens and an elevated risk of hyperglycaemia, possibly influenced by their effects on insulin sensitivity and glucose metabolism [10, 20]. The exact mechanisms behind these effects are not fully understood, as indicated by previous studies [8, 21]. In contrast, other studies have reported comparable metabolic outcomes or found no significant differences between DTG-based and non-DTG-based antiretroviral regimens [22, 23].

Inconsistent findings across studies coupled with varying screening services for PLWH [24] highlight the need for further studies in diverse settings like Ethiopia. Genetic, nutritional and socio-economic factors may also influence metabolic outcomes. Understanding the burden of hyperglycaemia and identifying modifiable risk factors are crucial for effective prevention and patient care [25]. With limited studies on the prevalence and association of hyperglycaemia with DTG-based regimens in Ethiopian healthcare settings, conducting further studies to explore this phenomenon is imperative to enhance the quality of care for this population. Thus, this study aimed to determine the prevalence and predictors of hyperglycaemia among adult PLWH on first-line ART for at least 12 months following the implementation of the test-and-treat strategy in Ethiopia.

2 | Methods

2.1 | Study Design, Setting and Population

This cross-sectional study was conducted from 5 January 2023 to 30 May 2024 among adult PLWH receiving follow-up care at health facilities in Hawassa City administration. The city administration is located in the Sidama Regional State of southern Ethiopia, located approximately 275 km from Ethiopia's capital, Addis Ababa. During the period of this study, eight healthcare facilities within the city administration offering ART services to more than 6300 PLWH. However, participants from two facilities were not included in the study due to personal preferences.

2.2 | Inclusion and Exclusion Criteria

This study included adults aged 18–65 years who initiated first-line ART after Ethiopia implemented the test-and-treat strategy in February 2017. Eligible participants were those who had received first-line ART for at least 12 months, achieved a viral load (HIV-ribonucleic acid [RNA]) level of < 1000 copies/ml and demonstrated at least fair adherence as described in the national HIV management guidelines [19]. The study also included individuals who initiated first-line ART with two nucleos(t)ide reverse transcriptase inhibitors (N(t)RTIs) as the backbone, combined with one NNRTI, and were either maintained on NNRTI-based regimens or later switched to a DTG-based regimen with the same backbone. Moreover, the study also included individuals who initiated and were maintained on two N(t)RTIs with a DTG-based regimen. However, we deliberately excluded participants on ART who had communication difficulties, experienced multiple treatment switches, were pregnant or lactating, were using antipsychotics or had critical illness, physical disabilities, liver disease or end-stage renal failure.

2.3 | Sample Size Determination and Sampling Technique

The sample size was determined using the single population proportion formula and calculated with Epi Info version 7.2 software, assuming a 95% confidence interval (CI), a significance level (α) of 5%, a margin of error of 0.05 and an anticipated DM incidence of 16% among PLWH on ART in Ethiopia [26].

The initial calculated sample size was 229, with a 10% adjustment for non-response. This study was part of a broader NCDs project with multiple objectives. The sample size of 279 determined based on a 23.9% prevalence rate for one of the NCDs [27] was larger than that calculated for hyperglycaemia, ensuring better representativeness for the overall evaluation of NCDs. Accounting for a design effect of 1.5 and an anticipated 10% non-response rate, we calculated the final sample size to be 465. Allocation was then based on the number of PLWH on first-line regimens at each facility. We calculated the sampling interval for each facility by dividing the number of PLWH on first-line ART by the allocated sample size. Participants were selected using a systematic random sampling method within each health facility.

2.4 | Data Collection and Procedure

Socio-demographic, socio-economic, clinical and other relevant data were collected using an interviewer-administered structured questionnaire. Trained nurses working in the respective ART clinics conducted the interviews and measurements. They also extracted relevant clinical data from participants' medical records.

2.5 | Variables and Measurement

2.5.1 | Dependent Variable

In this study, we defined hyperglycaemia among adults with HIV as the primary outcome variable, using a fasting blood glucose (FBG) level of ≥100 mg/dL, which includes both prediabetes and T2DM. We classified hyperglycaemia according to the guidelines from the American Diabetes Association (ADA), which have been adopted in the Clinical and Programmatic Management guidelines of Major NCDs in Ethiopia [28, 29]. Diabetes was diagnosed based on FBG ≥126 mg/dL, self-reported history and antidiabetic medication use or confirmed from medical records. Undiagnosed diabetes or newly diagnosed DM during this study was defined as FBG ≥126 mg/dL, confirmed by a repeat test of the same sample. Prediabetes (IFG) was defined by FBG levels between 100 and 125 mg/dL.

2.5.2 | Independent Variables

This study examined various predictors across multiple domains. Patient-related factors included sex, age, occupation, economic status, marital status, residence and education, along with anthropometric measurements such as weight, body mass index (BMI), waist and hip circumference (HC), waist–hip ratio (WHR), waist–height ratio (WHtR) and visceral fat level. Clinical and HIV-related factors considered were co-morbid conditions, baseline WHO disease stage, baseline functional status, opportunistic infections, duration since HIV diagnosis and mental health issues (anxiety, depression, insomnia, memory). Behavioural factors such as alcohol, cigarette and khat use as well as diet and physical activity were also assessed. Finally, treatment-related factors, including ART regimen type, treatment switches and duration since ART initiation, were evaluated as potential predictors.

Height was determined to the nearest 0.1cm using a stadiometer (Seca, Germany) with participants standing in the Frankfurt plane after removing shoes, hats and hair ornaments. The Omron Body Composition Monitor and Scale (Omron HBF-514C; Omron Healthcare Co. Ltd.) was utilised to assess participants' body weight, BMI and visceral fat level. This device employs bioelectrical impedance analysis (BIA) [30]. To measure body composition, each participant's age, height (in cm) and sex were entered into the device before they were instructed to step barefoot onto the scale. Data collectors instructed each participant to wear light clothes and stand barefoot on the scale, holding the display unit with both hands and extending their arms parallel to the floor while maintaining an upright posture. The device measures body composition by transmitting a painless, low-level electrical current through various body tissues. It directly measures weight and VF levels, whereas BMI was calculated via initially entered height information. The BMI of the participants was subsequently categorised as underweight (<18.5 kg/m^2), normal (18.5–24.99 kg/m^2), overweight (25.0–29.99 kg/m^2) or obese (≥30 kg/m^2) [31]. The visceral fat level was assessed in accordance with the Omron Healthcare manual [30].

WC and HC were measured to the nearest 0.1 cm. WC was measured in a horizontal plane, midway between the iliac crest and the costal margin, at the end of a normal expiration. While the HC was measured at the level of the greater trochanter via a non-stretchable tape measure [32]. The WHR and WHtR were then calculated by dividing WC by HC and WC by height respectively. Abdominal obesity was classified as a WC ≥94 cm for males and ≥80 cm for females or a WHR ≥0.90 for men and ≥0.85 for women. Additionally, a WHtR ≥0.5 was considered indicative of an increased risk of metabolic complications [33].

Participants' blood pressure (BP) and heart rate were assessed via a digital blood pressure monitor (Heuer digital sphygmomanometer) after 10 min resting in the data collection room. Two BP readings were taken at a 5-min interval. If the difference was greater than 5 mmHg, a third reading was obtained, and the average of the last two readings was recorded to determine the participant's BP status [34]. The International Physical Activity Questionnaire short form (IPAQ-SF) was employed to assess participants' physical activity levels. Activity levels were classified based on metabolic equivalents of task in minutes per week (MET-min/wk) as low (<600 MET-min/wk), moderate (600 to <3000 MET-min/wk) or high (≥3000 MET-min/wk) [35]. Participants were asked about their weekly frequency of fruit and vegetable (FAV) consumption, including the number of servings consumed on a typical day. Adequate FAV intake is defined by the WHO as the intake of 400–500 g/day, or approximately 5 servings (80 g each) [36]. Moreover, substance use was categorised as follows: participants who chewed khat, smoked cigarettes or consumed alcohol within the 30 days prior to the study were considered current users. Those with a history of using khat, cigarettes or alcohol at any point in their lifetime but who had not engaged in these behaviours in the past 30 days were

classified as former users [37]. Furthermore, anxiety and depression were assessed via a validated questionnaire (HADS) in the Amharic language for the Ethiopian population. It has seven questions each, and the responses are rated on a 4-point Likert scale, with a score of ≥ 8 indicating the presence of anxiety or depression [38, 39].

2.6 | Blood Sample Collection and Laboratory Analysis

Upon arrival at the ART clinic, all participants were asked whether they had fasted overnight (8–12 h), with the exception of water. Participants who had fasted were asked to provide a blood sample, while those who had eaten breakfast were advised to fast overnight (8–12 h) and return either the next day or at their next ART clinic visit to provide a sample. Then, overnight fasting blood was drawn from each participant in two separate test tubes: one in a gel-based serum separator tube with a clot activator and the other in an ethylene–diamine–tetraacetic acid (EDTA) anticoagulant containing tube. Both sample tubes were labelled with the participant's unique identification code. After collection, whole blood samples were kept at room temperature for a maximum of 20 min to allow clot formation and avoid glucose consumption through glycolysis [40–43]. The samples were promptly centrifuged at 3000 rpm for 8–10 min, allowing serum separation through a gel barrier. Subsequently the samples were analysed for FBG and lipid profiles, whereas EDTA blood was used for determination of glycated haemoglobin (HbA1c). If there was a delay in laboratory analysis, serum samples were promptly transferred to Nunc tubes labelled with participants' unique codes and stored at −20°C until analysis. Blood collection for HbA1c testing was prioritised for participants newly diagnosed with diabetes (FBG ≥ 126 mg/dL) due to the limited availability of reagents. The remaining HbA1c samples were stored in the deep fridge at −70°C. Lipid profiles were analysed using enzymatic colorimetric methods, FBG was assessed via the hexokinase UV method and HbA1c was measured using turbidimetric inhibition immunoassay (TINIA) on a Cobas 6000 series analyser with Roche reagents (Roche, Germany).

2.7 | Data Quality Management

The questionnaire was pretested on 46 similar adult participants at Leku General Hospital in the Sidama region and revised based on the feedback received. The questionnaire was checked daily to ensure consistency, completeness, clarity and accuracy of data collection. Nurses in the ART clinics received training on data collection and physical measurements. In addition, weight scales were calibrated daily against a standard calibrating tool before data collection. The physical measurements included at least two readings per participant and were averaged for reliability. Additionally, laboratory procedures were rigorously managed by Lab technologists in accordance with standard operating procedures (SOPs). Daily assessment of chemistry analyser was done performed to ensure precision of technical performance and reagent quality by running lyophilised quality control (QC) samples before the study samples. Furthermore, the principal investigator closely supervised the overall process to ensure data quality.

2.8 | Statistical Analysis

The data were entered into EpiData version 3.1 and exported to IBM SPSS version 27.0 for statistical analysis. Descriptive statistics, including means with standard deviation (SD), medians with interquartile ranges (IQRs) and percentages were computed to summarise participant characteristics. The normality of the data was assessed via histograms, Q–Q plots and the Kolmogorov–Smirnov test (K-S). The facility-level effect was insignificant, as indicated by an intra-class correlation coefficient (ICC) of 0.026, showing minimal variation between health facilities. Therefore, we opted to use a binary logistic regression model to examine the associations between hyperglycaemia and predictors. Independent variables with a $p < 0.25$ from the bivariate analysis were considered for inclusion in the multivariate analysis, along with variables identified in previous studies as risk factors for hyperglycaemia, regardless of their individual significance level in the bivariate analysis. Multi-collinearity of candidate variables was assessed, with those having a variance inflation factor (VIF) < 10 included in the final model. Model fit was evaluated using the Hosmer–Lemeshow test, where a $p > 0.05$ indicated a good fit. Adjusted odds ratio (AOR) and 95% CIs were used to measure the strength of associations between risk factors and outcomes.

3 | Results

3.1 | Socio-Demographic Features of the Study Participants

Out of 465 eligible adults, 443 participated in the study, with a response rate of 95.3%. More than half of the participants ($n = 259$, 58.5%) were women, with a mean age of 40.9 (SD, 9.6) years. The majority of the participants (68.4%) were 30–49 years old. Half of the participants were married and more than 41% had a monthly income of ≤ 2000 Ethiopian birr. In terms of education, 11.3% of participants had no formal education, while 57.1% had at least a secondary level education (Table 1).

3.2 | Physical Measurements, Behavioural Characteristics, Physical Activity Levels and Dietary Patterns of the Study Participants

The median time since HIV diagnosis was 4.2 (IQR, 2.3–6.1) years, while the mean duration on ART was 3.8 (SD, 1.9) years. The mean BMI of the study participants was 24.7 (SD, 4.8) kg/m^2. About 44.3% of participants had a BMI of ≥ 25 kg/m^2, with 31.2% classified as overweight and 13.1% as obese. Regarding self-reported substance use, 58.2% of participants reported ever-consuming alcohol, 37.7% had chewed khat and 14.5% had smoked cigarettes. In terms of physical activity, 32.3% of participants had inadequate physical activity, while 55.1% engaged in moderate physical activity. Only 10 (2.3%) and 15 (3.4%) respondents reported daily consumption of fruits and vegetables, respectively, while 35.4% did not consume any fruits and 9.9%

TABLE 1 | Socio-demographic features of the study population.

Variables	Category	Frequency	%
Sex	Female	259	58.5
	Male	184	41.5
Age	20–30 years	67	15.1
	31–40 years	172	38.8
	41–50 years	134	30.2
	50+ years	70	15.8
Residence	Rural	41	9.3
	Urban	402	90.7
Marital status	Single	47	10.6
	Married	222	50.1
	Divorced	102	23.0
	Widow/widower	72	16.3
Educational status	Not educated	50	11.3
	Informal	1	0.2
	Primary level	139	31.4
	Secondary level	128	28.9
	At least college	125	28.2
Occupation	Employed	190	42.9
	Farmers	10	2.3
	Merchants	89	20.1
	Unemployed	154	34.8
Monthly income in Ethiopian birr	< 5000 birr	276	62.3
	5000–10,000 birr	139	31.4
	> 10,000 birr	28	6.3

did not consume any vegetables in the week prior to the study (Table S1).

3.3 | Duration and Type of ART Regimens Used by the Study Participants

Initially, 218 (49.2%) participants began treatment with NNRTI-based first-line regimens; of these, 203 (93.1%) were subsequently transitioned to DTG-based first-line regimens. In addition, 225 (50.8%) participants initiated therapy with a DTG-based regimen and maintained it. At the time of the study, over 95% of the participants had been exposed to a DTG-based regimen, either as their initial treatment or following a switch.

3.4 | Overall Prevalence of Hyperglycaemia Among the Study Participants

The overall prevalence of hyperglycaemia was 24.4% (95% CI: 20.3–28.7). In men, it was 27.2% (95% CI: 21.2–33.7), while in women, it was 22.4% (95% CI: 17.0–27.4). Hyperglycaemic participants were older than those with normoglycaemia, with a mean age of 44.4 (SD, 9.3) years compared to 39.8 (SD, 9.5) years in the normoglycaemic group ($p < 0.001$). The prevalence of prediabetes and T2DM was 16.7% (95% CI: 13.1–20.3) and 7.7% (95% CI: 5.2–10.4) respectively. The prevalence of prediabetes among women was 18.5% (95% CI: 13.6–23.9), while 8.7% (95% CI: 4.9–13.0) had T2DM. In men, 15.4% (95% CI: 11.2–20.1) had prediabetes and 6.9% (95% CI: 3.9–10.0) were diagnosed with T2DM. Among the 34 participants diagnosed with T2DM, 28 (82.35%) were newly identified during this study (Figures 1 and 2).

3.5 | Factors Associated With Overall Hyperglycaemia and Diabetes Among the Study Population

After adjusting for confounding factors, individuals over 50 years of age had twice the odds of hyperglycaemia compared to those aged 50 or younger (AOR: 2.1; 95% CI: 1.1–3.9). The odds of hyperglycaemia were also twice as high among individuals who currently drink alcohol compared to those who do not (AOR: 2.1; 95% CI: 1.02–4.2). Individuals with a high WHR had 2.6 times greater odds of hyperglycaemia than those with a normal WHR (AOR: 2.6; 95% CI: 1.4–5.05). Moreover, individuals with a BMI $\geq 30\,kg/m^2$ had three times the odds of hyperglycaemia compared to those with a BMI $< 25\,kg/m^2$ (AOR: 3.2; 95% CI: 1.3–7.9) (Table 2).

The odds of developing T2DM was three times higher among individuals who currently drink alcohol than those who do not (AOR: 3.0; 95% CI: 1.1–8.4). Individuals with HIV and additional co-morbidities had 2.6 times higher odds of developing T2DM compared to those without co-morbidities (AOR: 2.6; 95% CI: 1.1–6.05). Additionally, individuals with a high WC had nearly eight times higher odds of DM compared to those with a normal WC (AOR: 7.5; 95% CI: 1.3–43.3). The odds of DM were three times greater among individuals with high triglycerides than those with normal triglyceride levels (AOR: 3.2; 95% CI: 1.3–7.7). However, DTG-based ART regimens did not show a significant association with T2DM when compared to EFV-based regimens (Table 3). Statistically significant interaction effects were observed between treatment regimens and age > 50 years, as well as between treatment regimens and BMI on hyperglycaemia (Table S2). Furthermore, sex-stratified analyses revealed significant interaction effects between DTG-based regimens and age > 50, overweight status and high triglyceride levels on hyperglycaemia (Table S3).

4 | Discussion

With limited research on the prevalence of hyperglycaemia and its association with first-line regimens, particularly those containing DTG, coupled with inconsistent findings, further studies are needed to address its extent and determinants in order to improve care and outcomes among PLWH. This cross-sectional study describes the prevalence and associated factors of hyperglycaemia among adult PLWH on first-line ART for at least 12 months following the implementation of the test-and-treat strategy in southern Ethiopia.

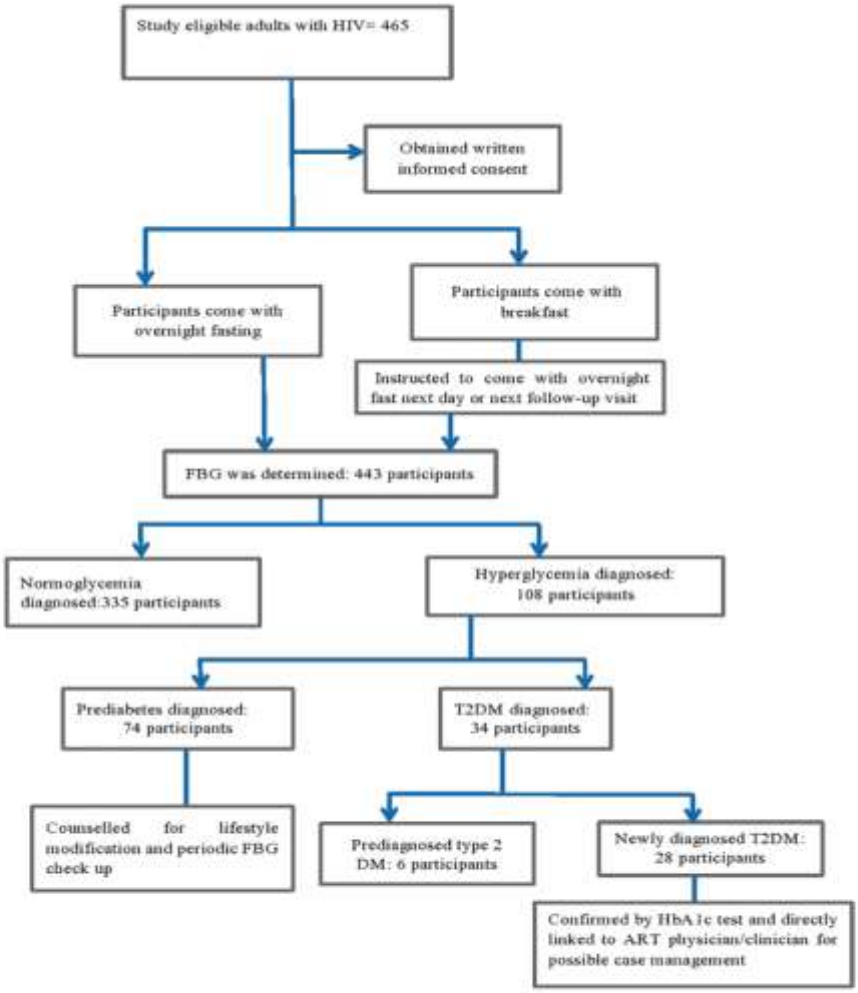


FIGURE 1 | Diagnostic categorisation and prevalence of hyperglycaemia among the study population.

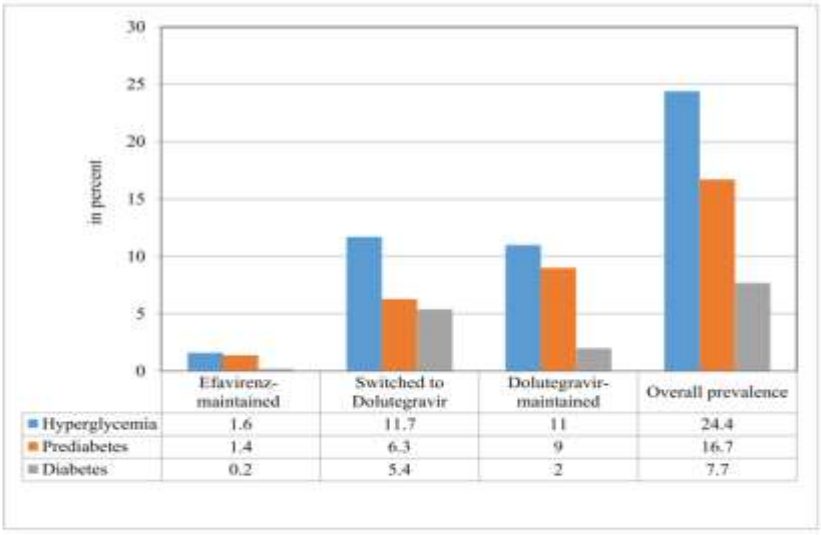


FIGURE 2 | Prevalence of overall hyperglycaemia, prediabetes and diabetes mellitus among the study population.

TABLE 2 | Factors associated with hyperglycaemia among the study population.

Variables	Category	Total $n = 443$	Hyperglycaemia, n (%)		COR (95% CI)	p	AOR (95% CI)	p
			Yes ($n = 108$)	No ($n = 335$)				
Age	≤ 50 years	373 (84.2)	80 (74.1)	293 (87.5)	1.00		1.00	
	> 50 years	70 (15.8)	28 (25.9)	42 (12.5)	2.4 (1.4–4.2)	< 0.001	2.1 (1.1–3.9)	0.021
Sex	Female	259 (58.5)	58 (53.7)	201 (60.0)	1.00		1.00	
	Male	184 (41.5)	50 (46.3)	134 (40.0)	1.3 (0.83–2.0)	0.249	0.98 (0.51–1.9)	0.948
Time since HIV diagnosis, years	Median (IQR)	4.2 (2.3–6.2)	4.4 (2.4–6.3)	4.2 (2.2–6)	1.05 (0.98–1.1)	0.169	0.99 (0.9–1.08)	0.816
Family history of diabetes	No	360 (81.3)	83 (76.9)	277 (82.7)	1.00		1.00	
	Yes	83 (18.7)	25 (23.1)	58 (17.3)	1.4 (0.85–2.4)	0.178	1.1 (0.63–2.05)	0.664
Treatment groups	Maintained on efavirenz	15 (3.4)	7 (6.5)	8 (2.4)	1.00		1.00	
	Switched to dolutegravir	203 (45.8)	52 (48.1)	151 (45.1)	0.39 (0.14–1.14)	0.085	0.46 (0.14–1.5)	0.204
	Maintained on dolutegravir	225 (50.8)	49 (45.4)	176 (52.5)	0.32 (0.11–0.92)	0.035	041 (0.12–1.4)	0.161
Received prophylaxis for OIs	No	151 (34.1)	42 (38.9)	109 (32.5)	1.00		1.00	
	Yes	292 (65.9)	66 (61.1)	226 (67.5)	0.76 (0.48–1.2)	0.227	0.69 (0.41–1.2)	0.163
Waist circumference	Normal	218 (49.2)	33 (30.6)	185 (55.2)	1.00		1.00	
	High	225 (50.8)	75 (69.4)	150 (44.8)	2.8 (1.7–4.4)	< 0.001	1.3 (0.53–3.0)	0.601
Waist–hip ratio	Normal	183 (41.3)	23 (21.3)	160 (47.8)	1.00		1.00	
	High	260 (58.7)	85 (78.7)	175 (52.2)	3.4 (2.0–5.6)	< 0.001	2.6 (1.4–5.05)	0.003
OIs other than TB	No	358 (80.8)	92 (85.2)	266 (79.4)	1.00		1.00	
	Yes	85 (19.2)	16 (14.8)	69 (20.6)	0.67 (0.37–1.2)	0.187	0.75 (0.39–1.4)	0.391
Alcohol intake	Never	185 (41.8)	37 (34.3)	148 (44.2)	1.00		1.00	
	Former	172 (38.8)	40 (37)	132 (39.4)	1.2 (0.73–2.0)	0.455	0.99 (0.54–1.8)	0.998
	Current	86 (19.4)	31 (28.7)	55 (16.4)	2.2 (1.3–4.0)	0.005	2.1 (1.02–4.2)	0.044
LDL-cholesterol	< 130 mg/dL	403 (91.0)	91 (84.3)	312 (93.1)	1.00		1.00	
	≥ 130 mg/dL	40 (9.0)	17 (15.7)	23 (6.9)	2.5 (1.3–4.9)	0.006	2.2 (1.02–4.6)	0.043
Days of fruit intake/week	Median (IQR)	1.0 (0–3)	2.0 (0–3)	1.0 (0–3)	1.1 (1.01–1.3)	0.033	1.1 (0.95–1.3)	0.197

(Continues)

TABLE 2 | (Continued)

Variables	Category	Total $n=443$	Hyperglycaemia, n (%)		COR (95% CI)	p	AOR (95% CI)	p
			Yes ($n=108$)	No ($n=335$)				
Days of vegetable intake	≥4 days/week	88 (19.9)	17 (15.7)	71 (21.2)	1.00		1.00	
	<4 days/week	355 (80.1)	91 (84.3)	264 (78.8)	1.4 (0.81–2.6)	0.219	1.8 (0.94–3.5)	0.074
Waist–height ratio	<0.5	156 (35.2)	22 (20.4)	134 (40.0)	1.00		1.00	
	≥0.5	287 (64.8)	86 (79.6)	201 (60.0)	2.6 (1.5–4.4)	<0.001	0.64 (0.26–1.6)	0.340
Body mass index	<25 kg/m²	247 (55.8)	40 (37.0)	207 (61.8)	1.00		1.00	
	25–29.9 kg/m²	138 (31.2)	43 (39.8)	95 (28.3)	2.3 (1.4–3.8)	<0.001	1.7 (0.79–3.5)	0.176
	≥30 kg/m²	58 (13.1)	25 (23.1)	33 (9.9)	3.9 (2.1–7.3)	<0.001	3.2 (1.3–7.9)	0.012
Monthly income in Ethiopian birr	<5000	276 (62.3)	56 (51.9)	220 (65.7)	1.00		1.00	
	5000–10,000	139 (31.4)	43 (39.8)	96 (28.7)	1.8 (1.1–2.8)	0.017	1.1 (0.66–1.9)	0.651
	>10,000	28 (6.3)	9 (8.3)	19 (5.7)	1.9 (0.8–4.3)	0.150	0.91 (0.32–2.6)	0.651
Physical activity performance status	High	56 (12.6)	8 (7.4)	48 (14.3)	1.00		1.00	
	Low	143 (32.3)	45 (41.7)	98 (29.3)	2.7 (1.2–6.3)	0.016	1.3 (0.52–3.4)	0.867
	Moderate	244 (55.1)	55 (50.9)	189 (56.4)	1.7 (0.8–3.9)	0.176	1.3 (0.55–3.1)	0.529

Note: High waist circumference: ≥94 cm in men and ≥80 cm in women; high waist–hip ratio: ≥0.90 in men and ≥0.85 in women.
Abbreviations: AOR, adjusted odds ratio; COR, crude odds ratio; dL, decilitre; IQR, interquartile range; kg, kilogram; LDL, low-density lipoprotein; m^2, square meter; mg, milligram; OIs, opportunistic infections; TB, tuberculosis.

TABLE 3 | Factors associated with diabetes mellitus among the study population.

Variables	Category	Total ($n=443$)	Diabetes mellitus, n (%)		COR (95% CI)	p	AOR (95% CI)	p
			Yes ($n=34$)	No ($n=409$)				
Age	≤50 years	373 (84.2)	25 (73.5)	348 (85.1)	1.00		1.00	
	>50 years	70 (15.8)	9 (26.5)	61 (14.9)	2.0 (0.9–4.6)	0.081	1.4 (0.50–3.9)	0.517
Treatment duration	<5 years	283 (63.9)	16 (47.1)	267 (65.3)	1.00		1.00	
	≥5 years	160 (36.1)	18 (52.9)	142 (34.7)	2.1 (1.05–4.2)	0.037	1.1 (0.37–3.1)	0.894
Time since HIV diagnosis, years	Median (IQR)	4.2 (2.3–6.2)	5.4 (3–6.7)	4 (2.2–6.0)	1.1 (1.01–1.2	0.026	1.01 (0.9–1.2)	0.875
Treatment groups	Maintained on efavirenz	15 (3.4)	1 (2.9)	14 (3.4)	1.00		1.00	
	Switched to dolutegravir	203 (45.8)	24 (70.6)	179 (43.8)	1.9 (0.2–14.9)	0.552	2.1 (0.2–22.7)	0.523
	Maintained on dolutegravir	225 (50.8)	9 (26.5)	216 (52.8)	0.6 (0.07–4.9)	0.621	0.69 (0.06–8.3)	0.771
Waist circumference	Normal	218 (49.2)	6 (17.6)	212 (51.8)	1.00		1.00	
	High	225 (50.8)	28 (82.4)	197 (48.2)	5 (2.0–12.4)	<0.001	7.5 (1.3–43.3)	0.024
Waist–hip ratio	Normal	183 (41.3)	4 (11.8)	179 (43.8)	1.00		1.00	
	High	260 (58.7)	30 (88.2)	230 (56.2)	5.8 (2.0–17)	<0.001	4.1 (1.02–16.2)	0.047
Anxiety/depression	No	425 (95.9)	31 (91.2)	394 (96.3)	1.00		1.00	
	Yes	18 (4.1)	3 (8.8)	15 (3.7)	2.5 (0.70–9.2)	0.157	2.9 (0.58–14.6)	0.192
Alcohol intake	Never	185 (41.8)	12 (35.3)	173 (42.3)	1.00		1.00	
	Former	172 (38.8)	8 (23.5)	164 (40.1)	0.7 (0.28–1.8)	0.453	0.54 (0.19–1.5)	0.251
	Current	86 (19.4)	14 (41.2)	72 (17.6)	2.8 (1.2–6.3)	0.014	3.0 (1.1–8.4)	0.037
Co-morbidity with HIV*	No	357 (80.6)	20 (58.8)	337 (82.4)	1.00		1.00	
	Yes	86 (19.4)	14 (41.2)	72 (17.6)	3.3 (1.6–6.8)	<0.001	2.6 (1.1–6.05)	0.03
Triglycerides	<150 mg/dL	292 (65.9)	13 (38.2)	279 (68.2)	1.00		1.00	
	≥150 mg/dL	151 (34.1)	21 (61.8)	130 (31.8)	3.5 (1.7–7.1)	<0.001	3.2 (1.3–7.7)	0.09
Cholesterol total	<200 mg/dL	386 (97.1)	27 (79.4)	359 (87.8)	1.00		1.00	
	≥200 mg/dL	57 (12.9)	7 (20.6)	50 (12.2)	1.8 (0.77–4.5)	0.168	0.83 (0.28–2.4)	0.833
Days of vegetable intake	≥4 days/week	355 (80.1)	30 (88.2)	325 (79.5)	1.00		1.00	
	<4 days/week	88 (19.9)	4 (11.8)	84 (20.5)	1.9 (0.66–5.6)	0.226	2.5 (0.77–8.5)	0.126

(Continues)

TABLE 3 | (Continued)

Variables	Category	Total (*n* = 443)	Diabetes mellitus, *n* (%)		COR (95% CI)	*p*	AOR (95% CI)	*p*
			Yes (*n* = 34)	No (*n* = 409)				
Waist–height ratio	< 0.5	156 (35.2)	5 (14.7)	141 (36.9)	1.00		1.00	
	≥ 0.5	287 (64.8)	29 (85.3)	258 (63.1)	3.4 (1.3–8.9)	0.014	0.19 (0.02–1.4)	0.105
Body mass index	< 25 kg/m^2	247 (55.8)	12 (35.3)	235 (57.5)	1.00		1.00	
	25–29.9 kg/m^2	138 (31.2)	16 (47.1)	122 (29.8)	2.6 (1.2–5.6)	0.018	0.96 (0.3–3.2)	0.947
	≥ 30 kg/m^2	58 (13.1)	6 (17.6)	52 (12.7)	2.3 (0.81–6.3)	0.119	1.2 (0.2–6.7)	0.864
Visceral fat level	Median (IQR)	4.2 (2.3–6.2)	8.3 (4.7–13)	5.4 (3–6.7)	1.1 (1.02–1.2)	0.013	0.94 (0.77–1.1)	0.581
Physical activity performance status	High	56 (12.6)	2 (5.9)	54 (13.2)	1.00		1.00	
	Insufficient	143 (32.3)	15 (44.1)	128 (31.3)	3.2 (0.7–14.3)	0.135	2.1 (0.38–12.1)	0.390
	Moderate	244 (55.1)	17 (50)	227 (55.5)	2.0 (0.45–9.0)	0.356	2 (0.37–11.2)	0.413

Note: High waist circumference: ≥ 94 cm in men and ≥ 80 cm in women; high waist–hip ratio: ≥ 0.90 in men and ≥ 0.85 in women.
Abbreviations: AOR, adjusted odds ratio; COR, crude odds ratio; dL, deciliter; IQR, interquartile range; kg, kilogram; m^2, square meter; mg, milligram.
[a]Coexistence of hypertension, cancer and or other chronic diseases with HIV.

The prevalence of hyperglycaemia among adult PLWH on ART in this study was 24.4%. This finding is aligned with the previous studies that were conducted in Ethiopia and Africa, showing hyperglycaemia prevalence rates between 18.5% and 28% [5, 8, 44]. However, the finding is higher than the hyperglycaemia rates reported in several studies among individuals on INSTI based and other ART regimens across Ethiopia: 7.9% in central Ethiopia [45], 14.7% in Tigray [46], 17.2% in Amhara [7] and 17.2% in Eastern Ethiopia [47]. Similarly, it is higher than the rates reported elsewhere, such as 15% in Zambia [48], 8.3% in Georgia [49] and 14.4% in the United States [50]. These inconsistencies may arise from differences in treatment duration, hyperglycaemia cutoffs (100 mg/dL vs. 110 mg/dL) and the varying effects of older versus newer ART regimens on glucose metabolism. Moreover, the finding is higher than the 12.4% prevalence reported in the 2015 National NCDs STEPS Survey of the general population in Ethiopia using ADA criteria and 7.1% using the WHO criteria [51]. This suggests that the factors contributing to hyperglycaemia in PLWH who are receiving ART may differ from those in the general population and may be influenced by factors such as HIV infection itself, HIV duration, immunosuppression and the effects of antiretroviral medication [52].

We found substantial rates of prediabetes (16.7%) and T2DM (7.7%) in this study. This is higher than the rate estimates reported for the general adult population in Ethiopia, which is 3.3% according to the IDF in 2021 [53] and 3.8% according to the WHO in 2016 [54]. Additionally, it is higher than the 2015 National NCDs STEPS Survey report, which revealed 9.1% for prediabetes and 3.3% for diabetes among adults in Ethiopia [51]. The differences in prediabetes and diabetes prevalence between our study population and the general population may be influenced by several factors. PLWH may be more vulnerable to health complications due to a compromised immune system, potentially leading to higher rates of prediabetes and T2DM. Additionally, medications used in HIV treatments have the potential to alter metabolism, influencing glucose regulation and increasing diabetes risk compared with the general population. Our findings also revealed higher rates of prediabetes and T2DM compared to previous studies conducted in PLWH: 14.2% prediabetes and 5% T2DM in Kenya [13], 13% prediabetes and 1.4% T2DM in the United States [50], 5.1% DM across Africa [5] and 10% prediabetes and 5% T2DM in Zambia [48]. The higher rates of prediabetes and T2DM observed in our study compared to the described studies may be attributable to several factors. Factors include the longer duration of DTG use in participants, regional and demographic variations in healthcare access [8], differences in diagnostic criteria [8] and disparities in healthcare infrastructure and diabetes screening practices [50].

In our study, 82.35% of diabetes cases were newly diagnosed, representing 6.3% of all participants. This rate surpasses the findings from similar studies such as 3.4% in Kenya [13] and 4.8% in rural South Africa [55]. Variations in lifestyles, inconsistent practices of HIV/NCD integrated services, diagnostic methods, NCD screening habits in ART clinics and limited self-screening habits could have contributed to disparities across studies and settings. The high prevalence of T2DM may highlight significant gaps in routine screening practices within ART clinics in our study population.

The use of DTG-based regimens was not associated with hyperglycaemia in this study. This finding is in line with the reports from previous studies that reported similar findings [22, 23]. In contrast, other reports suggest a potential association between the use of DTG-based regimens and an increased risk of hyperglycaemia, possibly due to its effects on insulin sensitivity and glucose metabolism [8]. This inconsistency may result from variations in participants' demographics and potential interactions with lifestyle factors.

In this study, obesity was significantly associated with hyperglycaemia. This finding is consistent with the literature, which has demonstrated a robust association between altered glucose metabolism and increased weight [7, 16]. The weight gains among those who received the DTG-based regimens [8] may exacerbate insulin resistance, compounded by synergistic metabolic effects with other ART medications and the presence of cardiometabolic problems, thereby contributing to dysglycaemia. Similarly, Rebeiro et al. [11] reported that initiating ART regimens with INSTIs rather than with NNRTIs may increase the risk of DM, potentially due to weight gain associated with INSTI use. In support of this, the majority of participants with hyperglycaemia (62.9%) and T2DM (64.7%) in our study had a BMI of $\geq 25\,kg/m^2$. Moreover, adjusted analyses in this study also revealed a significant interaction between DTG-based regimens and BMI in relation to hyperglycaemia, which may further support the results.

Our findings revealed an association between high WHR and hyperglycaemia, with the association of both elevated WHR and WC with T2DM. This finding is consistent with the reports of Njoroge et al., who highlighted the association between central adiposity and hyperglycaemia [13]. In support, elevated WHR and WC are indicative of central obesity that might impair insulin sensitivity and glucose metabolism, thereby increasing the risk of hyperglycaemia through inflammatory processes and hormonal disruption [56].

This study found a significant association between advanced age and hyperglycaemia. This is consistent with previous studies that have established an association between ageing and hyperglycaemia in PLWH [8, 57, 58]. Moreover, ageing might be linked to decreased insulin sensitivity due to physiological changes such as reduced muscle mass, impaired pancreatic β-cell function and increased chronic inflammation, which disrupts insulin signalling and glucose metabolism [59].

In this study, we observed an association between hyperglycaemia and alcohol consumption. This finding aligns with previous studies indicating that alcohol intake may increase the risk of developing hyperglycaemia or diabetes [60, 61]. Additionally, a correlation between alcohol consumption and the incidence of T2DM has been reported in men [62]. The underlying mechanisms are complex and may involve alcohol's impact on insulin activity and glucose metabolism.

We found a significant association between LDL cholesterol and hyperglycaemia, as well as between triglycerides and T2DM. Similarly, several studies have shown a positive association between blood glucose levels and both triglycerides [63] and LDL cholesterol levels [63, 64]. In addition, elderly individuals with hypertriglyceridaemia, hypercholesterolaemia and low HDL cholesterol are at an increased risk of developing diabetes [65]. This may be attributed to the synergistic effects of insulin resistance and ART-induced alterations in lipid metabolism, both of which contribute to the development and progression of hyperglycaemia and diabetes.

4.1 | Limitations

This study has several limitations: primarily its cross-sectional design, which restricts the ability to establish causal relationships between hyperglycaemia and its risk factors. The study focused on PLWH on ART without including HIV-negative individuals as a reference group. However, comparisons were made with findings from prevously published studies in the general adult population, highlighting higher rates of hyperglycaemia among PLWH on ART. Additionally, most participants were on DTG-based regimens, either through initiation or switching, resulting in an insufficient number of participants in the NNRTI-based arm for comparison during analysis. Despite these limitations, this study may offer valuable insights into the limited data setting of East Africa, particularly in Ethiopia.

5 | Conclusion

Our study found a higher prevalence of hyperglycaemia among PLWH compared to the general Ethiopian adult population, along with a significant rate of newly diagnosed T2DM. Modifiable risk factors contributing to hyperglycaemia included abdominal adiposity, BMI, dyslipidemia and alcohol intake. Non-modifiable risks included ageing and the presence of other co-morbidities with HIV. A significant interaction effect was observed between DTG-based regimens and age > 50 years, as well as between DTG-based regimens and BMI on hyperglycaemia.

The findings highlight potential gaps in routine screening and early detection of dysglycaemia in ART clinics, unless prompted by clients. Therefore, to improve early diagnosis and management, implementing routine screening protocols for all individuals on ART, regardless of symptoms, is highly recommended. Additionally, since most of the risk factors are modifiable, implementing targeted interventions focused on lifestyle and behavioural modifications for individuals with identified risk factors would be beneficial.

Author Contributions

Agete Tadewos Hirigo, Zelalem Debebe, Daniel Yilma and Ayalew Astatkie conceptualised and designed the study; conducted the data analysis and drafted the initial manuscript; contributed to data interpretation, critically revised the manuscript for intellectual content and provided final approval for publication. Agete Tadewos Hirigo was responsible for data collection. Zelalem Debebe, Daniel Yilma and Ayalew Astatkie supervised the study. All authors reviewed and approved the final manuscript.

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Ethics Statement

The study protocol was approved by the Institutional Review Board of the College of Natural and Computational Sciences at Addis Ababa University (approval No: IRB/07/14/2022). The participants were assured the freedom to withdraw from the study at any time without repercussions. Participants were not exposed to any harm, and no experimental risks were present. Throughout the study, participants' personal information was maintained with strict confidentiality.

Consent

The participants were fully informed about the research objectives and potential benefits, and then written consent was obtained from all participants.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data are not publicly accessible, but can be obtained upon reasonable request from the corresponding author.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section.

PAPER IV

The association between dolutegravir based first-line regimens and dyslipidemia among adults living with HIV on follow-up at health facilities in Hawassa city administration, Sidama region: a cross-sectional study

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Abstract

Background: Inconsistent evidence on lipid alterations in adults living with HIV on dolutegravir (DTG)-based antiretroviral therapy (ART) highlights the need for further study. This study aimed to assess the association between DTG-based regimens and dyslipidemia among adults on ART after the test-and-treat implementation in Ethiopia.

Methods: A cross-sectional study was conducted in the Hawassa City Administration, Sidama region, Ethiopia from January 2023 to May 2024. Participants were selected using systematic random sampling. Sociodemographic, clinical, and other relevant data were collected using a semi-structured questionnaire, supplemented by a review of medical records. Dyslipidaemia was classified based on the NCEP ATP III guidelines. A binary logistic regression model was fitted to identify factors associated with dyslipidemia. An adjusted odds ratio (aORs) and 95% confidence intervals (CIs) were computed to determine the strength of the association with statistical significance set at $p < 0.05$.

Results: Of the 465 eligible adults, 450 participated in the study, yielding a response rate of 96.8%. Of these, 262 (58.2%) were female. Overall, 74.0% (95% CI: 69.8%–78.0%) of participants had dyslipidemia, with a higher prevalence in males (79.8%) than females (69.8%). Low HDL-cholesterol (66.4%) was the most common lipid abnormality, followed by high TG and elevated total cholesterol/HDL-cholesterol ratio (each 34.2%). ART initiation with DTG-based regimen (aOR: 4.8; 95%CI: 1.2–18.5), increased waist circumference (aOR: 1.06; 95%CI: 1.01–1.11) and neck circumference (aOR: 1.2; 95%CI: 1.06–1.5) were significantly associated with dyslipidemia.

Conclusion: Initiating DTG-based first-line ART is significantly associated with dyslipidemia. It is kindly recommended that routine lipid monitoring be included in the clinical care of PLWH on ART to enable timely detection and management.

Keywords: Dyslipidemia, HIV, Antiretroviral therapy; Dolutegravir, Sidama region, Ethiopia

1. INTRODUCTION

Cardiovascular diseases (CVDs) are the most frequent causes of noncommunicable disease (NCD) deaths in Sub Sahara Africa (SSA), accounting for approximately 13% of all deaths and 37% of all NCD deaths (1, 2). In Ethiopia, the pooled prevalence of CVD is estimated at 5% (3). Among people living with HIV (PLWH), dyslipidemia represents the most prevalent CVD risk factor (4, 5), contributing to nearly 50% of their overall risk of developing CVD (6).

Dyslipidemia is characterized by abnormalities in lipid levels, including elevated triglycerides (TGs), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-c), and/or reduced high-density lipoprotein cholesterol (HDL-c) (7). These lipid abnormalities are influenced by a combination of immunological, hormonal, and genetic factors, as well as by specific antiretroviral therapy (ART) regimens (4). Among ART regimens, combinations of nucleos(t)ide reverse transcriptase inhibitors (N(t)RTIs) with efavirenz (EFV) have been linked to dyslipidemia, while protease inhibitor (PI)-based therapies tend to exert a more pronounced effect on lipid metabolism (8, 9). Additionally, ART regimens containing nevirapine have been associated with increased LDL-c levels, and long-term use of EFV has been connected to elevated TC and TG levels (10).

Studies investigating the relationship between integrase strand transfer inhibitors (INSTIs) and dyslipidemia have reported inconsistent findings. Some researches indicate that individuals on dolutegravir (DTG)-based regimens experience a higher incidence of dyslipidemia compared to those receiving non-nucleoside reverse transcriptase inhibitors (NNRTIs). Specifically, DTG-based ART has been associated with an increased risk of dyslipidemia-related complications (5, 11, 12), including a high incidence of low HDL-c (12) and elevated TGs (13). Furthermore, INSTIs are linked to increased TG levels and greater gains in both lean and fat mass, particularly in the trunk region, relative to NNRTIs, factors that contribute to an increased risk of obesity (14, 15). Notably, females on DTG-based regimens exhibit higher body fat percentages (BFP) compared to males on DTG and females on non-DTG regimens (16). Additional studies suggest that DTG-based regimens may elevate the risk of metabolic and cardiovascular complications compared to non-INSTI therapies (17).

Conversely, several studies have reported that dyslipidemia is less prevalent or even improved among individuals receiving INSTI-based regimens relative to those on non-INSTI regimens (18-20).

In addition, DTG has been highlighted as a valuable treatment option for older adults who may present with additional risk factors for metabolic syndrome or CVD (20).

DTG-based ART is widely utilized in HIV management; however, data on its effects on lipid metabolism among PLWH in East Africa, particularly in Ethiopia remain limited and not well explored. In addition, the impact of lipid profile changes following treatment initiation following the test-and-treat strategy has not been well characterized or adequately explored in this setting. Therefore, this study aimed to assess the association between DTG-based first-line regimens and dyslipidemia among adult PLWH receiving follow-up care at health facilities in Hawassa City Administration, Sidama region.

2. METHODS

2.1. Study population, setting and Design

This cross-sectional study was conducted between January 2023 and May 2024 in selected health facilities within the Hawassa City Administration, located in southern Ethiopia. Hawassa, the capital of the Sidama Region, is situated approximately 275 kilometers south of Addis Ababa, the capital city of Ethiopia. The study targeted adult PLWH who were receiving ART and attending routine follow-up visits at ART-providing health facilities in the city. At the time of the study, over 6,300 PLWH were receiving follow-up care across these facilities. Data were collected from six sites: Adare General Hospital, Hawassa University Comprehensive Specialized Hospital (HUCSH), Hawela-Tulla Hospital and three health centers (HCs): Bushulo HC, Millennium HC, and Tulla HC as illustrated in Figure 1.

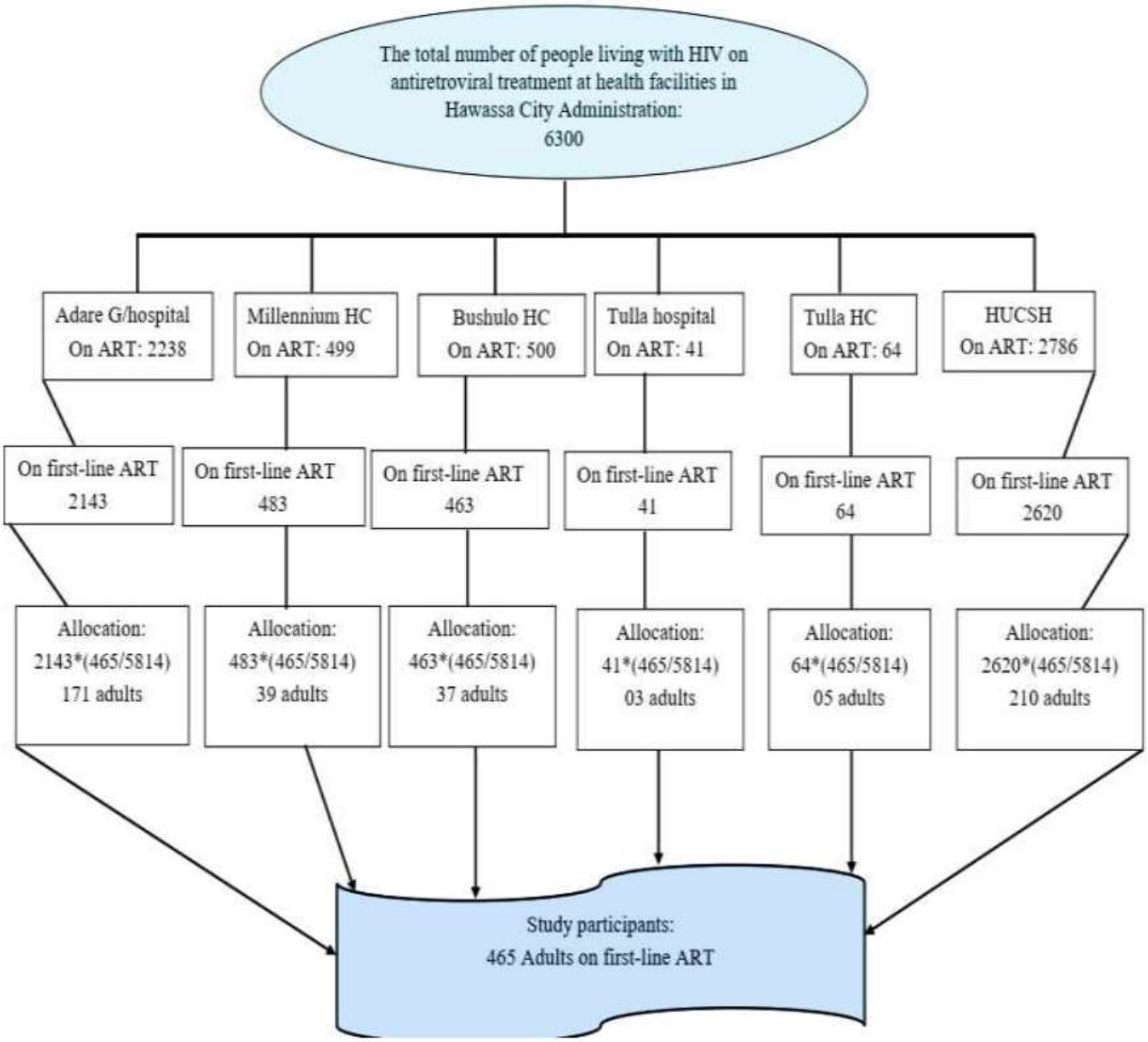


Figure 1 *Flowchart of the study population screening and enrolment*

2.2. Sample size and sampling techniques

Sample size estimation was performed using Epi Info version 7.2 and the single population proportion formula, with a 95% confidence interval (CI), 5% significance level (α), and 5% margin of error. Based on a reported dyslipidemia prevalence of 79.7% among PLWH on DTG-based first-line regimens in Ethiopia (5), an initial sample size of 277 was calculated, including a 10% allowance for non-response. However, since this study was part of a broader investigation of multiple NCDs, the sample size was recalculated using a lower prevalence estimate of 23.9% for one of the NCDs (21) to ensure greater representation. After adjusting for a 10% non-response rate, the sample size increased

to 310 and was further adjusted to 465 by applying a design effect of 1.5. The final sample size of 465 was proportionally allocated based on the number of individuals receiving first-line ART at each health facility (Figure 1). Participants were then selected using a systematic random sampling technique at each site.

2.3. Inclusion and exclusion criteria

This study included both males and females who met several criteria: they had to have started first-line ART after February 2017(following the rollout of the "test and treat" strategy in Ethiopia) and must have been on treatment for at least 12 months. Participants also had to be between 18 and 65 years old, actively involved in follow-up care and have achieved viral load suppression (HIV ribonucleic acid [HIV-RNA] <1000 copies/milliliter[mL]). The study enrolled adults in the following first-line regimen groups: those initiated on DTG-based therapy, those initiated and maintained on NNRTI-based therapy, and those who transitioned from NNRTI- to DTG-based therapy, as detailed in the previously published paper of this project (22).

However, participants were excluded if they had experienced more than one regimen switches, were pregnant or breastfeeding or had severe illnesses, chronic liver disease or end-stage renal failure.

2.4. Data collection tools and assessments

The data collection instrument was developed by adapting the World Health Organization (WHO) Stepwise Approach to NCD Surveillance questionnaire (23) and through a comprehensive review of relevant literature. The English version of the questionnaire included sections on sociodemographic characteristics, behavioral factors, physical measurements, dietary habits, laboratory tests, and both baseline and current clinical information. This questionnaire was translated into Amharic for data collection purposes. A pre-test was subsequently conducted on 46 adults living with HIV, and the questionnaire was refined based on the feedback obtained. Data collectors (nurses from ART clinics and laboratory technologists) received thorough training on data collection procedures, measurement techniques and participant approach interactions.

Data collectors conducted face-to-face interviews to obtain the required information and performed anthropometric and physical measurements. To ensure confidentiality, interviews were conducted in a private room within the health facilities. Additionally, an in-depth review of each participant's medical records was carried out to extract relevant clinical data. The principal investigator supervised data collection daily to ensure adherence to protocols and maintain data quality.

2.5.Variables

2.5.1. Dependent variable

The dependent variable, dyslipidemia, was defined according to the revised NCEP-ATP III guidelines, with the following criteria: TC ≥ 200 mg/dL, HDL-c < 40 mg/dL, LDL-c ≥ 130 mg/dL, TG ≥ 150 mg/dL, or a TC/HDL-c ratio ≥ 5 (24). Mixed dyslipidemia was defined as the presence of at least one abnormal lipoprotein along with one or more additional lipid abnormalities within an individual.

2.5.2. Independent variables

The independent variables were socio-demographic and economic factors included sex, age, occupation, monthly income, marital status, residence and education. Anthropometric and body composition measurements included body weight, body mass index (BMI), hip circumference (HC), neck circumference (NC), waist-to-hip ratio (WHR), waist-to-height ratio (WHtR), fat mass (FM), BFP, fat free mass (FFM), fat mass index (FMI), skeletal muscle mass and visceral fat (VF) levels. Clinical factors included blood pressure, fasting blood glucose (FBG) and self-reported recalling condition. Behavioral factors included alcohol use, smoking history and the level of physical activity performance. Dietary factors: fruits and vegetable consumption. HIV-related and treatment variables included time since HIV infection, WHO clinical stages, ART regimen type, prophylaxis treatment for opportunistic infections (OIs), treatment regimens switching and duration since ART initiation. Biological age and other relevant information were also considered as independent factors.

2.6. Measurements and assessments

After resting for 10 minutes in the data collection room, participants' blood pressure was measured, and hypertension status was classified according to clinical practice guidelines(25). Anthropometric data, including weight, height, NC and WC were measured according to the WHO stepwise approach (26). Height was measured using a stadiometer (Seca, Germany) with participants standing barefoot in the Frankfurt plane, wearing light clothing, and maintaining four contact points such as heels, buttocks, upper back, and back of the head against the stadiometer. Measurements were recorded to the nearest 0.1 cm. Omron HBF-514C bioelectrical impedance analysis (BIA) analyser was employed to measure or estimate body weight, FM (in kg), BFP, FFM (in kg), VF, biological age and percent skeletal muscle mass (27). The device reliability is high and correlates well with air displacement plethysmography (ADP) (28). Participants' age, height (in cm), and sex were entered into the device before they stepped barefoot onto the scale with their feet shoulder-width apart. They

were then instructed to hold the display unit with both hands extended parallel to the floor while standing upright. The Omron HBF-514C BIA provides measurements of body weight, BFP, VF and skeletal muscle, and calculates BMI using the recorded body weight and entered height. The instrument was daily calibrated for weight using standard calibrating tools. FM and FFM were then computed via BMI and BFP as follows: FM = weight × (BFP/100) and FFM = weight − [weight × (BFP/100)]. While FMI is calculated by dividing FM by the square of height (m^2), expressed as: FMI = FM (kg)/squared height (m^2). The VF level were classified as "Normal" (1–9; relative VF ≤ $300m^2$) or "High" (10–30; relative VF >$300m^2$) (27). Moreover, BFP and skeletal muscle were categorized based on age and sex of the participants and BFP categorized as "Normal" or "High," while percentage skeletal muscle was categorized as "Low" or "Normal to High" based on the Omron BIA manufacturer's guidelines (27). BMI was categorized based on the WHO classification (29).

Participants' physical activity levels were assessed using the International Physical Activity Questionnaire–Short Form (IPAQ-SF) and categorized as low, moderate, or high based on their responses (30). Due to practical limitations in accurately quantifying daily fruit and vegetable (FAV) intake by portion size (31), the frequency of FAV consumption, measured as the number of days per week was used as a proxy indicator of dietary intake.

2.7. Blood collection and laboratory analysis

Upon arrival at the ART clinic, participants were asked whether they had fasted overnight for 8–12 hours. Those who confirmed fasting provided a blood sample, while those who had eaten were instructed to fast and return the following day or at their next scheduled visit for sample collection. A 4–5 mL venous blood sample was collected from each participant using a gel-based serum separator tube (SST). The samples were kept at room temperature for no longer than 20 minutes to allow clot formation, then centrifuged immediately at 3000 revolutions per minute (rpm) for 8–10 minutes to separate the serum. Serum samples were analyzed for lipid profile and fasting blood glucose (FBG) levels. In cases of delayed analysis, the serum was transferred into Nunc tubes labelled with participants' unique codes and stored at −20°C until testing. Laboratory analysis was performed using the Cobas 6000 analyzer series, module c501 (Roche, Germany). The measurement of TC and TGs was done using an enzymatic colorimetric method (32, 33), while FBG was measured by a hexokinase UV method (34). Both HDL-c and LDL-c were measured using a direct homogeneous enzymatic assay (35, 36). Blood samples were collected and analyzed by laboratory technologists. Technical

performance and instrument accuracy were ensured by running quality control samples in accordance with standard operating procedures.

2.8. Statistical analysis

Data were visually inspected, cleaned, and entered into EpiData version 3.1, and statistical analyses were conducted using IBM SPSS Statistics version 27.0 (IBM Corp., Armonk, NY, USA). Categorical variables were summarized using frequencies and percentages, while continuous variables were described as means with standard deviations (SDs) for normally distributed data, or medians with interquartile ranges (IQRs) for non-normally distributed data. Depending on the distribution and type of variables, comparisons between groups were performed using the chi-square test, one-way ANOVA, Kruskal–Wallis test, independent t-test or Mann–Whitney U test, as appropriate. Binary logistic regression was employed to assess the association between DTG-based first-line regimens and other predictors with dyslipidemia. Candidate variables with a p-value < 0.25 in the bivariable analysis were assessed for multicollinearity using the variance inflation factor (VIF), with a VIF < 10 considered acceptable for inclusion in the multivariable logistic regression model. The model's goodness of fit was evaluated using the Hosmer–Lemeshow test, where a p-value > 0.05 indicated a good fit. Strength of associations were reported as adjusted odds ratios (aORs) with 95% confidence intervals (CIs), and variables with a p-value < 0.05 were considered statistically significant.

3. RESULTS

3.1. Sociodemographic and behavioral profiles of the study participants

Of the 465 eligible PLWH, 450 adults were included in the study, attaining a response rate of 96.8%. Females accounted for 58.2% (n = 262) of participants. The mean age of the participants was 41.1±9.7 years, ranges from 20-65 years (Table 1).

Table 1 Sociodemographic and other features of the study population

Characteristics	Category	Frequency (%)
Sex	female	262(58.2)
	Male	188(41.8)
Age , years	≤50 years	375(83.3)
	>50 years	75(16.7)
Residence	Rural	42(9.3)
	Urban	408(90.7)
Marital status	Single	47(10.4)
	Married	228(50.7)
	Divorced/widow	175(38.9)
Education	≤ primary level	191(42.4)
	Secondary level	133(29.6)
	College and above	126(28.0)
Occupation	Employed	194(43.1)
	Farmers	10(2.2)
	Merchants	91(20.2)
	Daily laborers	51(11.3)
	Housewife	49(10.9)
	No job and others	55(12.2)
Monthly income	<4000 birr	253(56.2)
in Ethiopian birr	≥4000 birr	197(43.8)
Religion	Orthodox	207(46)
	Protestant	191(42.4)
	Muslim	48(10.7)
	Catholic	4(0.9)
Alcohol intake	Not at all	188(41.8)
	Former	174(38.7)
	Current	88(19.6)
Smoking	Not at all	386(85.8)

	Former	54(12)
	Current	10(2.2)
Khat chewing	Not at all	280(62.2)
	Former	134(29.8)
	Current	36(8.0)
Physical exercise	Less active(<600 MET min/week)	146(32.4)
	Moderate active(600–2999 MET min/week)	248(55.1)
	High active(≥3000 MET min/week)	56(12.4)
Fruit	<4days	324(72)
intake/week	4-5days	110(24.4)
	6-7 days	16(3.6)
Vegetable	<4days	307(68.2)
intake/week	4-5days	116(27.8)
	6-7 days	27(6.0)

MET, Metabolic equivalents of task

3.2.Anthropometric, clinical and HIV-related profiles of the study population

The mean (±SD) of BMI and WC were 24.8 ±4.9 kg/m², and 85.9 ±12.5cm, respectively. Significant differences were observed between treatment groups in HC, WHtR, TC, percentage skeletal muscle and BFP (Table 2).

Among the participants, 202 (44.9%) had a BMI ≥25kg/m², 27 (6.0%) were classified as underweight and 134 (29.8%) had high WC. A review of participants' medical charts showed that 192 (42.7%) were in WHO clinical stage I at treatment initiation, while only 49 (10.9%) were in stage IV. A total of 288 (64%) participants had been on ART for less than five years and 298 (66.2%) had received prophylaxis for OIs. Additionally, 108 (24%) participants had a history of tuberculosis infection. Nearly half of the participants initiated NNRTI-based first-line regimens, comprising either zidovudine plus lamivudine (3TC) or tenofovir disoproxil fumarate (TDF) plus 3TC. More than half, however, were initiated on DTG-based first-line regimens, which included abacavir plus 3TC or TDF plus 3TC. Among those who started on NNRTI-based regimens, 92.3% (204/221) were subsequently switched to DTG-based regimens, while 7.7% (17/221) remained on their original NNRTI-based regimens.

Table 2 Body composition and clinical features of the study population

Characteristics	Category	Overall	Treatment groups		
			EFV-maintained	Switched to DTG	DTG-maintained
HIV duration, years [a]	Mean (SD)	4.7(3.1)	6.8(3.7)	6.3(2.5)	3.0(2.8)
ART duration, years [a]	Mean (SD)	3.8(1.9)	5.2(1.8)	5.4(1.0)	2.3(1.0)***
BMI, kg/m^2 [a]	Mean(SD)	24.8(4.9)	23.9(4.1)	25.2(4.8)	24.6(5.0)
WC, cm [a]	Mean(SD)	85.9(12.5)	88.4(14.1)	87.3(12.1)	84.5(12.6)
HC, cm [a]	Mean(SD)	95.6(10.4)	95.7(10.3)	97(10.5)	94.4(10.3)*
Waist-hip ratio [a]	Mean(SD)	0.89(0.1)	0.91(0.09)	0.9(0.1)	0.89(0.1)
Waist height ratio [a]	Mean(SD)	0.53(0.08)	0.52(0.07)	0.54(0.08)	0.52(0.08)*
Neck circumference [a]	Mean(SD)	32.7(2.9)	33.4(3.5)	32.7(3.1)	32.7(3.0)
Fasting glucose, mg/dL [a]	Mean(SD)	101.1(34.9)	98.9(11.2)	104.7(43.3)	98.1(26.4)
TC, mg/dL [a]	Mean(SD)	159.7(37.8)	175.2(37.1)	164.1(35)	154.6(39.6)**
TG, mg/dL [b]	Median(IQR)	119(88-176)	134(116-158)	119(86-173)	115(87-183)
LDL-c, mg/dL [a]	Mean(SD)	91.3(31)	107.1(27.7)	94.7(31.6)	87.1(30.1)
HDL-c, mg/dL [a]	Mean(SD)	36.7(9.7)	37(9.6)	37.8(9.6)	35.6(9.9)
TG/HDL-c ratio [b]	Median(IQR)	3.2(2.2-5.4)	4.1(2.8-4.9)	3.1(2.1-5.4)	3.2(2.2-5.7)
LDL/HDL-c ratio [a]	Mean(SD)	2.6(1.2)	3.0(0.9)	2.6(1.0)	2.6(1.4)
TC/HDL-c ratio [a]	Mean(SD)	4.6(1.7)	4.9(1.3)	4.6(1.4)	4.7(2.0)
Percentage skeletal muscle [a]	Mean(SD)	29.3(6.7)	30.4(6.0)	28.2(6.0)	30.2(7.1)**
Percentage body fat [a]	Mean(SD)	31.6(11.7)	29.3(10.3)	33.4(10.9)	30.2(12.3)*
Fat mass, kg [a]	Mean(SD)	21.4(10.7)	20.1(9.6)	22.6(10.2)	20.4(10.7)
Fat mass index, kg/m^2 [b]	Median(IQR)	7.8(5.2-7.8)	7.6(4.5-9.5)	8.1(6-11)	7.6(4.2-10.7)
Lean mass, kg [a]	Mean(SD)	43.9(9.1)	46.6(11.4)	43.3(9.1)	44.3(8.9)
Visceral fat level [a]	Mean(SD)	7.1(3.8)	7.6(4.0)	7.2(3.2)	7.0(4.3)

ART, antiretroviral therapy; BMI, body mass index; cm, centimeter; kg, kilogram; m^2, squared meter; LDL-c, LDL-cholesterol; HC, hip circumference; HDL-c, HDL-cholesterol; IQR: interquartile range; mg/dL, milligram/deciliter; SD, standard deviation; TC, total cholesterol; TG, triglyceride; WC, waist circumference; WHR, waist–hip ratio; WHtR, waist–height ratio; *, p<0.05; **, p<0.01; ***, p<0.001 (significance level: [a], one-way ANOVA; [b], Kruskal-Wallis test)

3.3. Patterns of dyslipidemia and body composition among the study population

Female participants had significantly higher mean levels of HDL-c, FM, and BFP (37.5 mg/dL, 25.1 kg, and 38.4%, respectively) compared to male participants (35.5 mg/dL, 16.3 kg, and 22.2%).

In contrast, males had higher mean values of FFM, VF, and median TGs compared to females. Overall, 333 (74.0%; 95% CI: 69.8–78.0) participants had at least one form of dyslipidemia according to the NCEP-ATP III guidelines (Table 3). According to the NCEP-ATP III criteria, 2.4%, 18.9%, 2.0%, and 66.4% of participants were classified as having high or very high cardiovascular risk based on TC, TGs, LDL-c, and HDL-c levels, respectively.

Table 3 Serum lipid profiles and body composition of the study population by sex

Characteristics	Total (n=450)	Male (n=188)	Female (n=262)	p value
Overall dyslipidemia: No	117(26.0%)	38(20.2%)	79(30.2%)	0.018 [a]
Yes	333(74.0%)	150(79.8%)	183(69.8%)	
Total cholesterol, mean (±SD)	159.7(37.8)	159.2(42.5)	160(34.1)	0.835[b]
< 200 mg/dl	391(86.9%)	154(81.9%)	237(90.5%)	0.008 [a]
≥ 200 mg/dl	59(13.1%)	34(18.1%)	25(9.5%)	
HDL-cholesterol, mean (±SD)	36.7(9.7)	35.5(9.8)	37.5(9.6)	0.03 [b]
<40 mg/dl	299(66.4%)	54(28.7%)	97(37.0%)	0.066 [a]
≥40 mg/dl	151(33.6%)	134(71.3%)	165(63.0%)	
LDL-cholesterol, mean(±SD)	91.3(31)	88.7(34)	93.2(28.4)	0.128 [b]
<130 mg/dl	409(90.9%)	169(89.9%)	240(91.6%)	0.534 [a]
≥130 mg/dl	41(9.1%)	19(10.1%)	22(8.4%)	
Triglycerides, median (IQR)	119(88-176)	132(96-132)	113.5(84-153)	<0.001[c]
<150 mg/dl	296(65.8%)	106(56.4%)	190(72.5%)	<0.001 [a]
≥150 mg/dl	154(34.2%)	82(43.6%)	72(27.5%)	
TC/HDL-cholesterol, mean (±SD)	4.6(1.7)	4.7(1.6)	4.5(1.7)	0.238 [b]
<5	296(65.8%)	111(59.0%)	185(70.6%)	0.011 [a]
≥5	154(34.2%)	77(41.0%)	77(29.4%)	
Visceral fat, mean (±SD)	7.1(3.8)	7.9(5.0)	6.5(2.5)	<0.001 [b]
Normal	344(76.4%)	117(62.2%)	227(86.6%)	<0.001 [a]
High	106(23.6%)	71(37.8%)	35(13.4%)	
Total fat mass (kg), mean (±SD)	21.4(10.7)	16.3(8.7)	25.1(10.5)	<0.001 [b]
Fat free mass (kg), mean (±SD)	43.9(9.1)	52.5(6.2)	37.8(4.8)	<0.001[b]
Total fat percent, mean (±SD)	31.6(11.7)	22.2(8.5)	38.4(8.6)	<0.001 [b]

Normal	150(33.3%)	80(42.6%)	70(26.7%)	<0.001 [a]
High	300(66.7%)	108(57.4%)	192(73.3%)	
Percentage skeletal muscle, mean(±SD)	29.3(6.7)	35.5(5.1)	24.8(3.1)	<0.001 [b]
Low	180(40.0%)	66(35.1%)	114(43.5%)	0.073 [a]
Normal to high	270(60.0%)	122(64.9%)	148(56.5%)	
Age (biological), years, mean (±SD)	42.6(14.4)	39.7(16.3)	44.6(14.4)	<0.001 [b]

TC, total cholesterol; HDL, high-density lipoprotein; LDL, low-density lipoprotein; SD, standard deviation (significance level: [a], chi-square test; [b], independent t-test; [c], Mann-Whitney U test)

The rate of dyslipidemia was higher among participants who initiated and remained on DTG-based regimens (40%) compared to those who switched to DTG-based regimens (31.6%) or those who remained on EFV-based regimens (2.4%) (Figure 2). Among participants with dyslipidemia, 38.6% had a single lipid abnormality, while 35.3% presented with mixed lipid abnormalities. Additionally, 31.5% of participants had two or three lipid abnormalities and 3.8% had all four. Low HDL-c was the predominant isolated dyslipidemia, observed in 34% of participants (Figure 3).

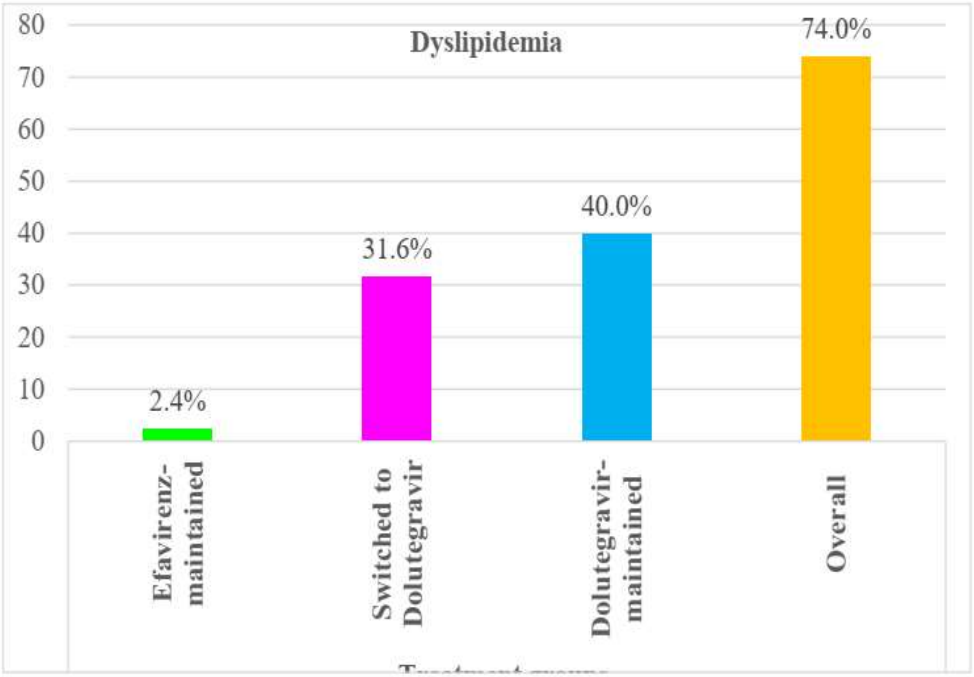


Figure 2 Patterns of dyslipidemia among the study population in relation to treatment regimens

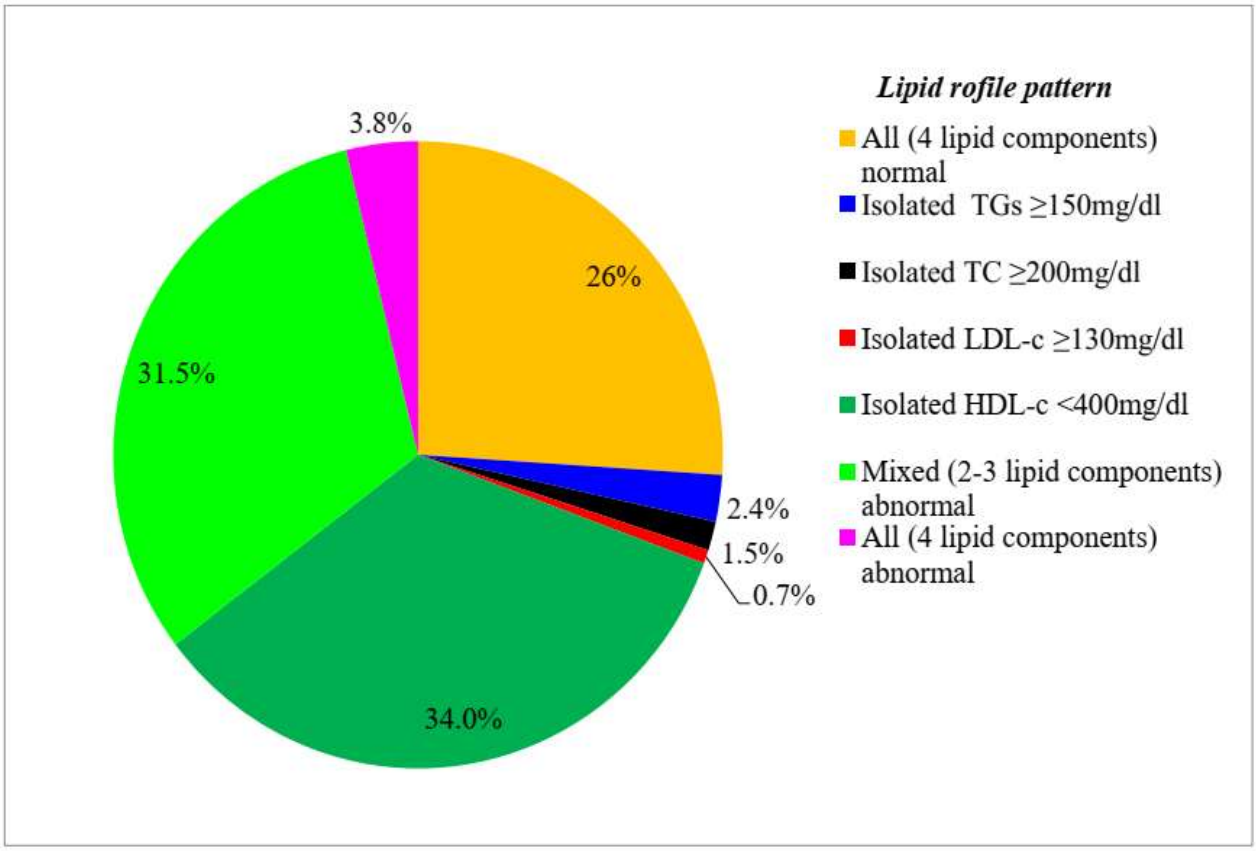


Figure 3 Proportions of isolated and mixed dyslipidemia within single individual among the study population

3.4. Factors associated with dyslipidemia among the study population

In the crude analysis, dyslipidemia was associated with male sex, age over 50 years, low physical activity, blood pressure ≥130/85 mmHg, baseline WHO clinical stage IV, BMI, NC, VF, use of prophylaxis for OIs, WC, biological age, and FBG. After adjusting for covariates in the multivariable analysis, treatment initiation with a DTG-based regimen, NC, and WC remained significantly associated with dyslipidemia (Table 4).

Table 4 Factors associated with dyslipidemia among the study population

Characteristic	Category	Total n(%)	Dyslipidemia Yes, n(%)	cOR(95%CI)	aOR(95%CI)
Sex	Females	262(58.2)	183(40.7)	1.00	1.00
	Male	188(41.8)	150(33.3)	1.7(1.1-2.6)*	0.44(0.17-1.2)
Age	≤50 years	375(83.3)	270(60.0)	1.00	1.00
	>50 years	75(16.7)	63(14.0)	2.0(1.06-3.9)*	1.6(0.71-3.7)
Monthly income in	< 4000 birr	253(56.2)	181(40.2)	1.00	1.00
Ethiopian birr	≥ 4000 birr	197(43.8)	152(33.8)	1.3(0.87-2.1)	0.75(0.45-1.3)
Alcohol intake	Never	188(41.8)	132(29.3)	1.00	1.00
	Ever drunk	262(58.2)	201(44.7)	1.4(0.91-2.1)	0.97(0.58-1.6)
Recalling problem	No	318(70.7)	241(53.6)	1.00	1.00
	Yes	132(29.3)	92(20.4)	0.73(0.47-1.1)	0.62(0.37-1.02)
Physical activity	Moderate-high	304(67.6)	120(26.7)	1.00	1.00
	Low active	146(32.4)	213(47.3)	1.97(1.2-3.2)**	1.4(0.82-2.5)
Treatment duration	< 5 years	288(64.0)	221(49.1)	1.00	1.00
	≥ 5 years	162(36.0)	112(24.9)	0.68(0.44-1.0)	1.1(0.87-1.4)
Regimens	maintained on efavirenz	17(3.8)	11(2.4)	1.00	1.00
	switched to dolutegravir	204(45.3)	142(31.6)	1.2(0.44-3.5)	1.8(0.57-5.9)
	maintained on dolutegravir	229(50.9)	180(40.0)	2(0.71-5.7)	4.8(1.2-18.5)*
Blood pressure, mmHg	<130/85	307(68.2)	217(48.2)	1.00	1.00
	≥130/85	143(31.8)	116(25.8)	1.78(1.1-2.9)*	1.2(0.72-2.1)
Baseline WHO clinical stage	Stage I	192(42.7)	133(29.6)	1.00	1.00
	Stage II	89(19.8)	70(15.6)	1.6(0.9-2.9)	1.5(0.79-2.8)
	Stage III	120(26.7)	88(19.6)	1.2(0.73-2.0)	0.93(0.51-1.7)
	Stage IV	49(10.9)	42(9.3)	2.7(1.1-6.3)*	1.8(0.7-4.7)
Body mass index, kg/m^2	Mean(SD)	24.8(4.9)	25.1(4.9)	1.05(1.01-1.1)*	0.9(0.79-1.03)
Waist circumference, cm	Mean(SD)	85.9(12.5)	87.4(12.6)	1.8(1.1-3.0)*	1.06(1.01-1.11)*
Neck circumference, cm	Mean(SD)	32.7(2.9)	33.1(3.2)	1.2(1.1-1.3)***	1.2(1.06-1.5)*
Visceral fat level	Normal	344(76.4)	243(54.0)	1.00	1.00
	High	106(23.6)	90(20.0)	2.3(1.3-4.2)**	0.9(0.37-2.2)

Body fat level	Normal	150(33.3)	104(23.1)	1.00	1.00
	High	300(66.7)	229(50.9)	1.4(0.92-2.2)	0.99(0.46-2.1)
Percentage skeletal muscle	Normal-high	270(60.0)	192(42.7)	1.00	1.00
	Low	180(40.0)	141(31.3)	1.5(0.94-2.3)	1.05(0.56-2.0)
Prophylaxis for OIs	Not received	152(33.8)	103(22.9)	1.00	1.00
	Received	298(66.2)	230(51.1)	1.6(1.04-2.5)*	1.3(0.78-2.2)
Biological age	Mean(SD)	42.6(14.4)	43.7(15.3)	1.02(1.01-1.03)*	0.99(0.94-1.03)
Fasting blood glucose	Mean(SD)	101.1(34.9)	103.1(38.2)	1.01(1.0-1.02)*	1.00(0.99-1.01)

Biological age (biological age indicates the rate of physical ageing in the body); aOR, adjusted odds ratio; cOR, crude odds ratio; cm, centimetre; OIs, opportunistic infections; mmHg, millimetre of mercury; SD, standard deviation; WHO, World Health Organization; *, $p<0.05$; **, $p<0.01$; ***, $p<0.001$

4. DISCUSSION

The overall prevalence of dyslipidemia in this study was 74%. Low HDL-c was the most frequently observed lipid abnormality, whereas TC and LDL-c abnormalities were less common. Sex-specific analysis revealed a higher prevalence of dyslipidemia among males compared to females. Additionally, initiation of treatment with DTG-based regimens, as well as increased WC and NC, were significantly associated with dyslipidemia.

We found that 74% of adults on first-line ART had at least one dyslipidemia according to the NCEP ATP III criteria. This finding is comparable to rates reported in previous studies conducted in Ethiopia and other African countries, including a 72% prevalence in southwest Ethiopia (37), 77.34% in north Ethiopia (38), 74.8% in central Ethiopia (39), 78% in Uganda (11) and 77.5% in Tanzania (40). In contrast, it is higher than rates reported in several other Ethiopian studies, such as 59.9% in north Shewa, Ethiopia (41), 69.7% and 69.3% in systematic reviews from Ethiopia (42, 43), 48.4% among individuals on DTG-based regimens in southwest Ethiopia (44), 55.2% in central Ethiopia (45) and 63.9% in northwest Ethiopia (46). The observed variations may be explained by factors including differences in the effects of ART regimens on lipid metabolism, the duration of ART exposure, and the consequent alterations in lipid profiles.

The prevalence of TC dyslipidemia in this study was 13.1%, which is consistent with the 12% reported in Uganda (11). However, this rate is notably lower than those reported in several other studies conducted in similar populations, such as 47.3% in north Shewa, Ethiopia (41); 39.08% and 39.78% in systematic reviews from Ethiopia (42, 43); 34.2% in northwest Ethiopia (46); and

45.9% and 22.6% in central Ethiopia (39, 45). Evaluating the impact of ART on lipid profiles remains challenging due to significant variability among different ART drug classes, differences within the same class, and the complexity of multidrug HIV treatment regimens (37). DTG-based regimens have demonstrated favourable effect on TC levels compared to earlier-generation ART agents, such as NNRTIs and PIs(19). This may partly explain the comparatively lower prevalence of TC dyslipidemia observed in the present study.

In this study, the prevalence of low HDL-c was 66.4%, indicating nearly 7 out of 10 individuals had low HDL-c. This is consistent with prevalence rates reported in other studies, which ranged from 63% to 68.5% (5, 12, 47, 48). However, the prevalence observed in our study was lower than that reported in other studies, which ranged from 71.3% to 72.1% (37, 49). Notably, those studies applied sex-specific thresholds for low HDL-c (<40 mg/dL for males and <50 mg/dL for females) (50), which is more high for females than the uniform <40 mg/dL cut-off recommended by the NCEP-ATP III guidelines (24) and used in our study. The higher prevalence in those studies is likely attributable to these differing classification criteria.

In the present study, LDL-c dyslipidemia was observed in 9.1% of PLWH, which is comparable to findings from Uganda (11) and China (51). However, this rate is markedly lower than those documented in several African studies, including Ethiopia where LDL-c dyslipidemia prevalence ranged from 20.3% to 59.8% (5, 39, 40, 43, 44, 46, 52). Variations in prior ART exposure and regional factors such as diet, lifestyle, healthcare access, genetics and environment may underlie differences in LDL-c levels. Despite the lower prevalence of LDL-c dyslipidemia in this study, increased total and visceral fat, particularly in the trunk, may still elevate future cardiovascular risk (53).

Several studies have reported elevated TG levels in PLWH on first-line ART, ranging from 13.1% to 50% (5, 11, 39-41, 44-46, 54). Similarly, our study found a prevalence of 34.2%.

We observed a 34.2% prevalence of elevated TC/HDL-c ratios. This marker has been strongly associated with increased risk of stroke, acute myocardial infarction and arterial stiffness in prior studies (55-57). Importantly, an elevated TC/HDL-c ratio may indicate heightened cardiovascular risk even when LDL-c levels appear within normal or desirable ranges (56, 58).

Treatment initiation with DTG-based regimens was significantly associated with dyslipidemia in this study. This association is consistent with evidence from cohort studies indicating that INSTIs, including DTG, are more likely to cause lipid abnormalities compared to NNRTIs (13,

19, 59). This positive association may be attributed to the combined effects of aging, HIV-related pathophysiology, and ART-induced alterations in lipid metabolism (40). Even though DTG is favoured for its high genetic barrier to resistance and better virological outcomes, its potential metabolic side effects require careful consideration in clinical decision-making. In addition, INSTIs are generally associated with a significantly lower risk of dyslipidemia than ritonavir-boosted PIs (18-20, 60-63), their risk remains significantly higher compared to NNRTI-based regimens. Prior PI exposure may have elevated baseline lipid levels, potentially confounding the association between current DTG use and dyslipidemia. This highlights the importance of distinguishing treatment-naïve from treatment-experienced individuals when evaluating metabolic outcomes related to ART. Additionally, variations in study design, population characteristics and duration of DTG exposure likely contribute to the heterogeneity observed in lipid profile findings across studies.

In this study, each 1 cm increase in WC was associated with a 6% increase in dyslipidemia, which is consistent with previous reports identifying elevated abdominal obesity as a contributing factor to dyslipidemia and other cardiometabolic disorders (15, 61). This association likely reflects the impact of central adiposity, which may promote insulin resistance, systemic inflammation, and altered lipid metabolism. Additionally, each 1 cm increase in NC was significantly associated with a 20% increase in dyslipidemia risk. Similarly, other studies have identified NC as an important cardiovascular risk factor for dyslipidemia (64, 65) and a robust predictor of atherogenic dyslipidemia beyond traditional measures of central obesity (66).

5. Strengths and limitations of the study

This study has several notable strengths. By focusing on individuals who initiated first-line ART under Ethiopia's "test and treat" policy, it provides timely and relevant insights into current treatment outcomes. The use of systematic sampling enhanced the representativeness of PLWH across the selected health facilities. Restricting inclusion to participants on ART for at least 12 months ensured adequate exposure to assess effects on lipid profiles. Moreover, excluding individuals with multiple regimen switches minimized potential confounding from treatment-related dyslipidemia.

However, this study has some limitations. The use of face-to-face interviews may have introduced social desirability bias, potentially affecting the accuracy of self-reported data. The

cross-sectional design limits the ability to infer causal relationships between dyslipidemia and associated factors. In addition, this study excluded pregnant women, severely ill patients and individuals with multiple ART regimen switches to minimize clinical heterogeneity and confounding factors. Consequently, these exclusions may limit the generalizability of our findings to the broader population of people living with HIV. Moreover, baseline lipid profiles were unavailable, as lipid measurements were not routinely performed or documented in medical records, thereby constraining the assessment of changes from baseline lipid levels.

6. CONCLUSION

A substantial proportion of PLWH on first-line ART had dyslipidemia, with low HDL-c being the most frequently observed lipid abnormality. Dyslipidemia was associated with DTG-based regimens, along with increased WC and NC (markers of central and upper-body adiposity). The significant associations between dyslipidemia, DTG-based regimens and altered body fat distribution suggest an elevated risk of cardiometabolic complications in this population. These findings highlight the importance of lipid profile assessments both at baseline and periodically along with body fat distribution, to effectively manage metabolic risks in PLWH. Additionally, important to balance post treatment metabolic risks of DTG-based regimens with their therapeutic benefits. Future research is encouraged to employ well-controlled, longitudinal studies to comprehensively investigate the long-term effects of DTG-based regimens on lipid metabolism, taking into account baseline lipid profiles, prior ART exposure and potential sex-specific differences, in order to better understand their metabolic impact and associated cardiovascular risks and to inform clinical decision-making.

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Contributors

ATH, ZD, DY and AA conceptualized and designed the study. ATH and AA[#] were responsible for data collection and laboratory analysis. ZD, DY and AA did supervision throughout the study. ATH, ZD, DY and AA conducted the data analysis, drafted the initial manuscript, contributed to data interpretation, critically revised the manuscript for intellectual content and gave final approval for publication. All authors reviewed and approved the final manuscript.

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Competing interests

The authors declare that they have no competing interests.

Ethics approval

The Institutional Review Board of the College of Natural and Computational Sciences at Addis Ababa University study approved the study (approval No: IRB/07/14/2022). Participants were fully informed about the research objectives and potential benefits and written consent was obtained from all participants. The study adhered to the principles outlined in the Declaration of Helsinki. They were assured of their right to withdraw from the study at any time without any consequences.

Data availability statement

The datasets generated during and/or analysed during the current study are available from the corresponding author upon reasonable request.

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PAPER V

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Prevalence and determinants of metabolic syndrome among adults living with HIV on first-line antiretroviral treatment in southern Ethiopia: a cross-sectional study

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Abstract

Background: Antiretroviral therapy (ART) has significantly reduced morbidity and mortality among people living with HIV (PLWH). However, data on the burden of metabolic syndrome (MetS) in sub-Saharan Africa remains limited, particularly following the implementation of universal test-and-treat strategies and the widespread use of integrase inhibitor-based combinations.
Objective: This study aimed to determine the prevalence and associated factors of MetS among adults receiving first-line ART in the Hawassa City Administration, southern Ethiopia.
Design: A cross-sectional study.
Methods: The study was conducted from January 2023 to May 2024, adapting the World Health Organization (WHO) stepwise approach to collect data. All study-relevant data were collected from participants using a pretested structured questionnaire. MetS was defined according to the 2009 harmonized criteria. A binary logistic regression analysis was conducted to identify predictors of MetS, with adjusted odds ratio (aOR) and 95% confidence intervals (CIs).
Results: A total of 450 adults participated in the study, of whom 262 (58.2%) were females. The mean (standard deviation) age of the participants was 41.1(±9.7) years. The prevalence of MetS was 36.4% (95% CI: 32.2–41.6), with low high-density lipoprotein (HDL) cholesterol as the most frequent component observed in 368 (81.8%) participants. Age >50 years (aOR: 2.9; 95% CI: 1.4–6.2), alcohol use (aOR: 2.7; 95% CI: 1.2–6.4), body mass index ⩾25 kg/m² (aOR: 3.7; 95% CI: 1.9–7.1), triglyceride/HDL-cholesterol ratio (aOR: 1.5; 95% CI: 1.3–1.7), family history of hypertension (aOR: 2.1; 95% CI: 1.1–3.8), and high waist-height ratio (aOR: 5.4; 95% CI: 1.8–15.9) were significantly associated with MetS. However, dolutegravir-based first-line regimens were not significantly associated with MetS (p=0.482 for DTG initiation, and p=0.34 for switching to DTG).
Conclusion: The noticeable prevalence of MetS among PLWH highlights its potential to increase cardiovascular risks. Therefore, routine screening of PLWH for components of MetS is essential to reduce the health risks associated with metabolic disorders. As most of the identified risk factors are modifiable, implementing lifestyle interventions is also imperative.

Plain language summary

Prevalence and determinants of metabolic syndrome among adults living with HIV on first-line antiretroviral treatment in southern Ethiopia

In this study, we investigated the prevalence and determinants of metabolic syndrome (MetS) in adults with HIV on antiretroviral therapy in southern Ethiopia. We presented the prevalence of MetS and its key risk factors in this population. We observed a high prevalence of MetS, with low HDL cholesterol being the most frequently observed component. We also

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identified that older age, alcohol use, high body mass index, triglyceride/HDL cholesterol ratio, family history of hypertension and increased waist-height ratio were significantly associated with MetS. We found no significant association between dolutegravir-based regimens and MetS. Therefore, we recommend routine screening for MetS components and proactive management of related conditions. In addition, most of the identified risk factors are modifiable, interventions focused on diet, weight management and alcohol use could help reduce MetS in this population. Further studies are required to investigate additional underlying factors and the long-term metabolic risks associated with antiretroviral therapy.

Keywords: adults, first-line antiretroviral therapy, HIV, metabolic syndrome, southern Ethiopia

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Introduction

Metabolic syndrome (MetS) is characterized by a cluster of risk factors for cardiovascular diseases (CVDs) and metabolic disorders, which include abdominal obesity, high triglycerides (TGs), low high-density lipoprotein cholesterol (HDL-c), raised blood pressure or hypertension, hyperglycemia or diabetes mellitus, and insulin resistance (IR).[1,2] Evidence indicates that individuals with MetS are at significantly increased risk of cardiovascular-related morbidity and mortality.[3,4]

Antiretroviral therapy (ART) has significantly improved life expectancy and reduced HIV/aquired immunodeficiency syndrome (AIDS)-related morbidity and mortality among people living with HIV (PLWH). However, along with this succsess, the prevalence of MetS is also rising in this population, posing individuals at significant risk for non-communicable diseases (NCDs).[5] Recent reports have indicated a significant prevalence of MetS among PLWH globally and in sub-Saharan Africa (SSA).[6,7] A global meta-analysis estimated the pooled prevalence of MetS in PLWH to be 25.3% (95% CI: 22.9–27.6), with a higher rate of 25.6% (95% CI: 23.0–28.2) among those who received ART compared to 18.5% (95% CI: 15.5–21.4) in ART untreated individuals.[6] In SSA, studies reported a prevalence of MetS among PLWH of 23.3% (95% CI: 18.8–27.8)[5] and 21.5% (95% CI: 15.1–26.8),[8] both of which surpass the 12.0% (95% CI: 5.0–21.0) prevalence rate reported in individuals without HIV.[8]

In Ethiopia, studies have reported the prevalence of MetS as 21.7% (95% CI: 19.36–24.0) using the National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III) criteria, and 29.91% (95% CI: 21.54–38.28) using the International Diabetes Federation (IDF) criteria.[9] These rates were higher than those reported among the working adult population in Ethiopia, where the prevalence was 18.45% (95% CI: 13.89–23.01)[10] and 20.1% (95% CI: 17.8–22.4).[11] The development of MetS is complex and multifactorial, influenced by a range of contributing factors such as obesity,[12–15] female sex,[14] the use of protease inhibitor (PI)-based ART regimens[12] and the duration of ART exposure.[12]

In 2018, the integrase strand transfer inhibitors, particularly dolutegravir (DTG), were endorsed by the World Health Organization (WHO) as the preferred treatment option for PLWH.[16] Since then, DTG-based regimens have been widely distributed across SSA, including Ethiopia, substituting non-nucleoside reverse transcriptase inhibitors (NNRTIs) and PI-based ART regimens.[15] However, evidence regarding the effect of DTG-based regimens on MetS is inconsistent, with some studies raising concerns about metabolic issues associated with DTG,[17] such as dyslipidemia,[18,19] elevated blood pressure,[20,21] clinical weight gain[22,23] and hyperglycemia.[24,25] In contrast, other studies have reported a protective effect or reduced risk of metabolic dysregulation with the use of DTG-based regimens.[26]

Early identification of cardiometabolic burden and its modifiable risk factors is essential for the prevention and management of cardiovascular risks among PLWH on ART, as evidenced by reliable epidemiological findings. However, there is a scarcity of data regarding individuals who initiated ART after the adoption of the universal test-and-treat strategy in Ethiopia, coupled with the widespread use of first-line DTG- based regimens that contain DTG. Therefore, this study aimed to determine the prevalence and associated factors of MetS among adults who initiated first-line ART and had been on treatment for at least 12 months in southern Ethiopia following the implementation of the test-and-treat strategy.

Materials and methods

Study setting, design, and study population

This cross-sectional study was conducted from January 5, 2023 to May 30, 2024 at health facilities in the Hawassa City Administration. Hawassa, the capital of the Sidama Region in southern Ethiopia, is 275 km away from Addis Ababa, the capital of Ethiopia. Eight health facilities in the city administration are providing ART services to over 6300 PLWH during the study period. The eligible participants were adult PLWH aged 18–65 years who had initiated ART and were actively receiving follow-up care at health facilities in the city administration.

Inclusion and exclusion criteria

This study included adults aged 18–65 years who initiated first-line ART after the implementation of the test-and-treat strategy in Ethiopia. In addition, participants had been on first-line ART for at least 12 months, achieved viral load suppression (HIV–ribonucleic acid (HIV–RNA)) below 1000 copies/milliliter, and demonstrated at least fair adherence to ART. Regarding first-line ART regimens, the study included individuals who initially started a regimen comprising two nucleos(t)ide reverse transcriptase inhibitors (N(t)RTIs) and one NNRTI and continued on this regimen (NNRTI-maintained group). It also included those who began with two N(t)RTIs plus one NNRTI and later switched to a regimen of two N(t)RTIs plus DTG (switched to the DTG group). Moreover, individuals who initiated and remained on a regimen of two N(t)RTIs plus DTG (DTG-maintained group) were included in the study. However, the study specifically excluded participants on first-line ART with a history of more than one treatment switch, as well as those who were pregnant or breastfeeding within the first 6 months of the study. In addition, participants who were critically ill or physically disabled, those with known liver or renal failure, and individuals with active opportunistic or severe infectious diseases were also excluded.

Sample size and sampling techniques

The sample size was calculated using Epi-Info version 7.2 developed by Centers for Disease Control and Prevention (CDC), based on a 23.9% prevalence of MetS among PLWH in SSA,[5] with a 5% margin of error and a 1.96 *z*-value for a 95% confidence interval (CI). In addition, risk factors significantly associated with MetS were considered to compute a maximally representative sample size,[15,27] accounting for a 95% CI, 80% power, a 1:1 exposed-to-unexposed ratio, and odds ratio (OR). A sample size of 279 was calculated based on a prevalence of 23.9%. After adjusting for a 10% nonresponse rate and a design effect of 1.5, the final sample size was determined to be 465. This sample size was selected as it was considered larger and more representative of the study objectives than the sample size computed based on MetS risk factors. The sample size of 465 was proportionally allocated across each health facility based on the number of PLWH receiving first-line regimens at the respective study sites. Subsequently, a systematic random sampling technique was conducted to recruit study participants.

Data collection questionnaire

The data collection questionnaire was adapted from the WHO Stepwise Approach to Chronic Disease Risk Factor Surveillance tool[28] and recently published literature on MetS. The questionnaire was first developed in English and then translated into the Amharic language. It covers the following sections: sociodemographic and economic factors (such as sex, age, occupation, monthly income, marital status, residence, and education); anthropometric and related measurements (body weight, body mass index (BMI), waist circumference (WC), hip circumference (HC), neck circumference (NC), waist-to-hip ratio (WHR), waist-to-height ratio (WHtR), fat mass and visceral fat levels); clinical factors

(comorbid conditions, self-reported recalling problem and family history of hypertension and diabetes); behavioral factors (alcohol use, smoking history, and level of physical activity and engagement); and HIV and its treatment-related variables (time since HIV infection, ART regimen type, treatment switches and the duration since ART initiation) and other relevant information. All data were collected by trained and experienced nurses and laboratory technologists working in the ART clinics of the respective health facilities.

Assessments and measurements

Sociodemographic, economic, anthropometric, body composition, clinical, behavioral, and other relevant data were collected through participant interviews and the review of their medical records using a pretested structured questionnaires. After a minimum of 10 min of rest in the data collection room, participants' blood pressure was measured using a digital blood pressure monitor. This blood pressure apparatus has a diagnostic accuracy of ±3 mm of mercury (mmHg) for blood pressure and ±5% for pulse rate. Two readings were taken within a 5-min interval and the average was recorded. If the difference between the initial two readings exceeded 5 mmHg, a third reading was taken and the average of the last two readings was then recorded to assess the blood pressure status of each participant.

The WHO Stepwise approach was applied to collect data on body weight, height, and WC.[29] Body weight, visceral fat level (1–30 range), and body fat percentage (BFP) were measured using the Omron Full Body Sensor Body Composition Monitor with Scale (Omron HBF-514C; Omron Healthcare Ltd.). Measurements with this Omron bioelectrical impedance analyzer (BIA) were conducted in accordance with the manufacturer's guidelines.[30] Standing height of the participants was measured with a Seca stadiometer (Hamburg, Germany) to the nearest 0.1 cm. Participants' weight and height were measured while they stood barefoot and dressed in light clothing. BMI (in kg/m^2) was calculated using the BIA during weight measurement by inputting each individual's respective height into the device. The BMI was then categorized as underweight (<18.5 kg/m^2), normal weight (18.5–24.9 kg/m^2), overweight (25–29.9 kg/m^2), and obesity (≥30 kg/m^2).[31] While fat mass was calculated from body weight and BFP as ((weight × BFP)/100).

WC and HC measurements were taken using a non-stretchable measuring tape and recorded to the nearest 0.1 cm. The WHR and WHtR were calculated by dividing WC by HC and WC by height, respectively.[32] Abdominal obesity was defined as a WC ≥94 cm for males and ≥80 cm for females, a WHR >0.90 in men and >0.85 in women, or a WHtR ≥0.5.[32] NC was measured while participants stood upright with their arms relaxed at their sides. The head was positioned in the Frankfort horizontal plane, and the measurement was taken at the midpoint of the cervical spine and the mid-anterior neck, perpendicular to the neck's long axis, just below the Adam's apple for males.[33]

Regarding substance use, current alcohol consumption and smoking refer to individuals who engaged in each behavior at least once during the month prior to the study. Ever alcohol drinking, smoking, and khat use denote respondents who have used each substance at any point in their lifetime.[34] In addition, the short form of the International Physical Activity Questionnaire (IPAQ) was used to assess participants' physical activity levels. Total activity was measured in metabolic equivalent of task (MET)-minutes per week and categorized as low (<600 MET-min/week), moderate (600 to <3000 MET-min/week), or high (≥3000 MET-min/week).[35]

Blood sample collection, processing, and laboratory analysis

About 4–5 mL of venous blood was collected from each participant after an overnight fasting of 8–12 h. The samples were drawn into gel-based serum separator tubes, with each tube carefully labeled using the participant's unique identification code. The blood samples were then left undisturbed at room temperature for a maximum of 20 min to allow for clot formation. Following this, they were promptly centrifuged at 3000 rotation per min (rpm) for 8–10 min. This process enabled serum separation from cells via a gel barrier, effectively creating a stable barrier between the two layers. Then, the serum samples were either analyzed promptly or transferred into Nunc tubes labeled with participants' unique code and stored in the deep freezer at −20°C in the Hawassa University Comprehensive Specialized Hospital laboratory in case of a 1- or 2-week delay in laboratory analysis. The fasting blood glucose (FBG) and lipid profiles were analyzed using the Cobas

6000 series biochemistry analyzer (Roche diagnostics, Germany). TGs were measured using an enzymatic colorimetric method, FBG was measured with the hexokinase UV method, and HDL-c level was determined using a direct homogeneous enzymatic assay. Both blood samples collection and laboratory analysis were performed by trained laboratory technologists.

Outcome variable of the study

The primary outcome variable in this study was the prevalence of MetS among adults living with HIV who were on first-line ART. It is defined according to the 2009 harmonized criteria established by the Joint Interim Statement (JIS). A diagnosis of MetS in an individual requires the presence of at least three of the following components: (1) TGs ⩾150 mg/dL or treatment for high TGs; (2) HDL-c <40 mg/dL in males or <50 mg/dL in females, or treatment for low HDL-c; (3) BP ⩾130/85 mmHg or previously diagnosed hypertension or treatment with antihypertensive medication; (4) FBG ⩾100 mg/dL or previously diagnosed diabetes or treatment for high glucose; and (5) WC ⩾80 cm in females or ⩾94 cm in males.[4]

Ensuring data quality

The questionnaire was initially developed in English and then translated into Amharic by a bilingual translator. Prior to data collection, a pretest was conducted on 46 the questionnaires, and necessary amendments were made based on the feedback obtained during the pretest. Data collectors received training before the study commenced. Test tube labels were cross-checked with participants' unique identification numbers, and blood samples collection was carefully performed, including proper tourniquet application to prevent hemolysis. All laboratory procedures were executed in accordance with standard operating procedures. All data collection activities were overseen by the principal investigator.

Statistical analysis

Descriptive statistics were used to summarize the study participants across different variables. The chi-square test was used to assess the significance of categorical variables, while the independent *t*-test and Mann–Whitney *U* test were used to compare continuous quantitative data between study groups. In addition, binary logistic regression analysis was performed to evaluate the association between independent factors and the study outcome. Variables with a *p*-value <.20 in the bivariablete analysis were included in the multivariable analysis. In addition, variables such as sex and ART regimens, which have been previously identified as risk factors for MetS were included in the final model regardless of their significance in the bivariate analysis. Prior to multivariable analysis, multicollinearity was assessed using a variance inflation factor (VIF) to identify linear associations between predictors. variable with a VIF threshold of less than 10 were considered acceptable for this analysis. Whereas model fit was evaluated with the Hosmer–Lemeshow test, where a *p*-value >0.05 indicates a good fit. The strength of associations between the outcome and explanatory variables was reported using adjusted ORs (aORs) and 95% CI, with a *p*-value of <0.05 considered statistically significant. Data were entered into EpiData 3.1 and statistical analysis was performed using IBM Statistical Package for the Social Sciences (SPSS) Statistics version 27.0 (IBM Corp., Armonk, NY, USA).

Results

Sociodemographic and behavioral characteristics of the study participants

Of 465 eligible adult PLWH, 450 participated in the study (with a 96.8% response rate). Among the participants, 262 (58.2%) were female, and more than half were married. The majority of participants were resided in urban areas, and 262 (58.2%) reported alcohol consumption. Regarding nutritional status, nearly one-third were classified as overweight, while 61(13.5%) were categorized as obese (Table 1).

Anthropometric and clinical characteristics of the study participants

The mean age of the participants was 41.1 (standard deviation: 9.7) years and females were significantly younger than males. Females had significantly higher mean BMI, HC, HDL-c, and median fat mass compared to males. On the contrary, males had significantly increased mean systolic and diastolic blood pressure, WHR, NC, and median TG/HDL-c, visceral fat, and TGs than females. However, mean WC, FBG, and

Table 1. Characteristics of adult people living with HIV on antiretroviral treatment.

Parameters	Total, frequency (*n*)	Percent (%)
Age		
20–29 Years	51	11.3
30–39 Years	153	34.2
40–49 Years	147	33.4
⩾50 Years	86	21.1
Body mass index (kg/m²)		
<18.5	27	6.0
18.5–24.9	221	49.1
25–29.9	141	31.3
⩾30	61	13.6
Residence		
Rural	42	9.3
Urban	408	90.7
Marital status		
Single	47	10.4
Married	228	50.7
Divorced/Widow/ widower	175	38.9
Education		
Unable to read and write	50	11.1
Primary	141	31.3
Secondary	133	29.6
Tertiary	126	28
Occupation		
Farmers	10	2.2
Employed	194	43.1
Merchants	91	20.2
Housewife	49	10.9
Daily laborers	51	11.4
No work	55	12.2
Monthly income in Ethiopian birr		
⩽2000 birr	184	40.9
2001–4000 birr	91	20.2
4001–6000 birr	80	17.8
⩾6001 birr	95	21.1
Alcohol intake status		
Not at all	188	41.8
Former	174	38.7
Current	88	19.5
Ever smoked cigarette		
Not at all	386	85.8
Yes	64	14.2
Physical exercise		
Low	146	32.4
Moderate active	248	55.1
High active	56	12.4

Physical activity (low: <600 MET-min/week; moderate: 600 to <3000 MET-min/week and high: ⩾3000 MET-min/week).

ART duration did not show significant variation between sexes (Table 2).

Two hundred twenty nine (50.6%) participants initiated DTG-based first-line ART regimens, while 221 (49.4%) participants initiated treatment with NNRTI-based first-line regimens, both with a similar backbone of two N(t)RTIs. Among those who initially started with NNRTI-based regimens, 204 of 221 (92.3%) were later switched to DTG-based first-line regimens, while 17 of 221 (7.7%) continued with NNRTI-based regimens.

Prevalence of MetS and its components

According to the 2009 harmonized (JIS) criteria, 422 (93.8%) participants had at least one component of MetS, with 81(18%) having three, 61 (13.6%) having four, and 22 (4.9%) having five

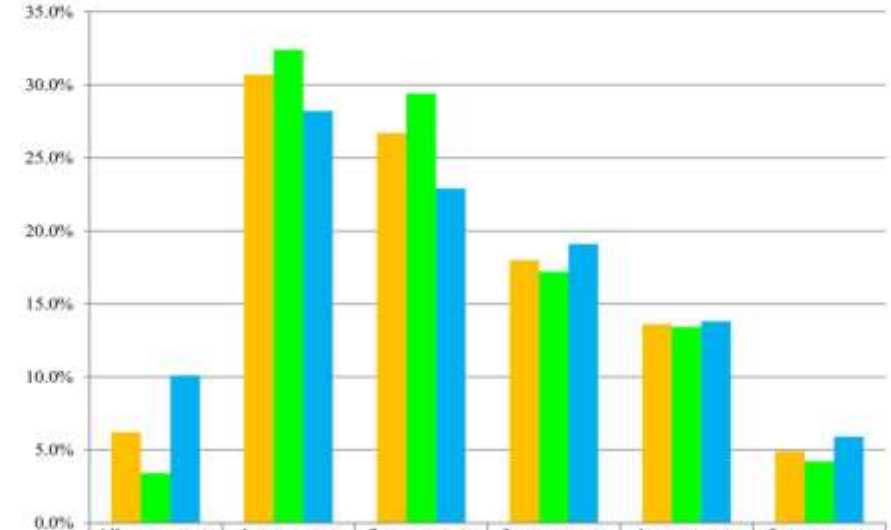
Table 2. Anthropometric and clinical characteristics of adult people living with HIV on antiretroviral treatment.

Parameters	Total (n = 450)	Female (n = 262)	Male (n = 188)	p-Value
Age, years	41.1 (9.7)	39.4 (8.9)	43.4 (10.3)	<0.001*
Weight, kg	65.4 (13.9)	62.9 (13.7)	68.9 (13.5)	<0.001*
BMI, kg/m²	24.8 (4.8)	25.6 (5.3)	23.7 (3.9)	<0.001*
Waist circumference, cm	85.9 (12.5)	85.3 (12.7)	86.8 (12.1)	0.253*
Hip circumference, cm	95.7 (10.4)	98.2 (10.7)	92.3 (8.9)	<0.001*
Waist-hip ratio	0.9 (0.1)	0.87 (0.09)	0.94 (0.09)	<0.001*
Waist-height ratio	0.53 (0.08)	0.54 (0.08)	0.51 (0.07)	<0.001*
Systolic blood pressure, mmHg	118.6 (17.9)	115 (16.6)	123.4 (18.5)	<0.001*
Diastolic blood pressure, mmHg	77.5 (12.5)	76.2 (11.5)	79.3 (13.6)	0.029*
Fasting blood glucose, mg/dL	101 (34.9)	99.2 (30.2)	104 (40.5)	0.115*
HDL-c, mg/dL	36.7 (9.7)	37.5 (9.6)	35.5 (9.8)	<0.001*
Triglycerides, mg/dL[a]	119 (88–175.7)	113 (84.2–153)	132 (96–218)	<0.001**
HIV infection duration, years[a]	4.2 (2.3–6.1)	4.5 (2.6–6.6)	3.5 (2.0–5.6)	<0.001**
ART duration, years	3.8 (1.9)	4.0 (1.9)	3.6 (1.9)	0.061*
Neck circumference, cm	32.7 (3)	31.1 (2.2)	35 (2.4)	<0.001*
Triglyceride/HDL-c ratio[a]	3.2 (2.2–5.4)	3 (2.0–4.9)	4 (2.5–6.6)	<0.001**
Fat mass, kg[a]	20.5 (13.7–27.9)	24 (17.3–31.3)	16 (9.1–22.3)	<0.001**
Visceral fat level (1–30 range)[a]	7 (5–9)	6 (5–8)	7 (4–11)	0.011**

[a]Values are presented as median (interquartile range), while all other variables are presented as mean (standard deviation).
Significance: *independent t-test; **Mann–Whitney U test.
mmHg, millimeter of mercury.

components of MetS. The prevalence of two components of MetS was 29.4% (77/262) among female participants, accounting for 17.1% of all participants, and 22.9% (43/188) among male participants, representing 9.6% of all participants (Figure 1). Overall, 164 participants had MetS with a prevalence of 36.4% (95% CI: 32.2–41.6). Of the 164 participants with MetS, 73 (44.5%) were males and 91 (55.5%) were females. In terms of age groups, 42.7% (95% CI: 35.3–51.3) of participants aged 40–49 years and 54.7% (95% CI: 44.2–64.2) of those aged ⩾50 years had MetS (Figure 2). In addition, 62.4% (95% CI: 55–69.3) of participants with a BMI ⩾25 kg/m² had MetS. Among the 164 total cases of MetS: 79 (48.25%) were individuals who initiated and remained on a DTG-based regimen, while 77 (47%) were transitioned from an NNRTI-based first-line regimen to DTG, and 8 (4.9%) initiated and continued on NNRTI (EFV)-based regimen (Figure 3). Moreover, 15 (3.3%) participants on the efavirenz-based regimen, 165 (36.7%) who switched to a DTG-based regimen, and 188 (41.8%) who remained on the DTG-based regimen had low HDL-c (Figure S1).

The prevalence of individual components of MetS was as follows: 220 (44.4%) for high WC, 110 (24.4%) for raised FBG, 154 (34.2%) for high TGs, 143 (31.8%) for elevated blood



	All components normal	1 component abnormal	2 components abnormal	3 components abnormal	4 components abnormal	5 components abnormal
	Metabolic syndrome components					
Total	6.2%	30.7%	26.7%	18.0%	13.6%	4.9%
Females	3.4%	32.4%	29.4%	17.2%	13.4%	4.2%
Males	10.1%	28.2%	22.9%	19.1%	13.8%	5.9%

Figure 1. Overview of the metabolic syndrome components in study participants stratified by sex.

pressure, and 368 (81.8%) for low HDL-c. In addition, females had significantly higher rates of abdominal obesity (51.5% vs 34.6%), low HDL-c (89.3% vs 71.3%), and high WHtR (70% vs 58%) compared to males, respectively. In contrast, males had significantly higher rates of elevated blood pressure (39.4% vs 26.3%), high TGs (43.6% vs 27.5%), and high WHR (69.1% vs 57.3%) compared to females, respectively (Table 3).

Factors associated with MetS

We found that age >50 years, alcohol consumption, BMI ⩾25 kg/m², TG/HDL-c ratio, high WHtR, and a family history of hypertension were significantly associated with the prevalence of MetS. In contrast, DTG-based first-line regimens did not show a significant association with MetS when compared to NNRTI (efavirenz)-based regimens (Table 4).

Discussion

MetS was prevalent among adults on ART in southern Ethiopia, with a rate of 36.4% (95% CI: 32.2–41.6). Factors significantly associated with MetS included older age, alcohol consumption, BMI, high WHtR, a family history of hypertension, and a high TG/HDL-c. The use of DTG-based regimens did not show a significant association with MetS compared to those on efavirenz-based regimens.

The overall prevalence of MetS in the study was 36.4%, which is higher than the rates reported in systematic reviews and cross-sectional studies conducted in similar populations both globally and in Africa, where the prevalence ranged from 18.0% to 29.91% using IDF criteria,[9,10,36,37] 18.1% to 34.89% using ATP III criteria[9,10,36,37] and from 13.9% to 33.1% using JIS.[15,18,27,38,39] The finding was also higher than the prevalence reported among apparently healthy working adults in Ethiopia[10,11,40] as well as in community-based and public servant studies,[41,42] which ranged from 11.9% to 27.6% according to the IDF[11,40–43] and from 11.2% to 18.5% according to ATP III.[10,40–43] The discrepancies may be attributed to variations in diagnostic criteria, study timeframes, the effects of ART regimens on metabolic and

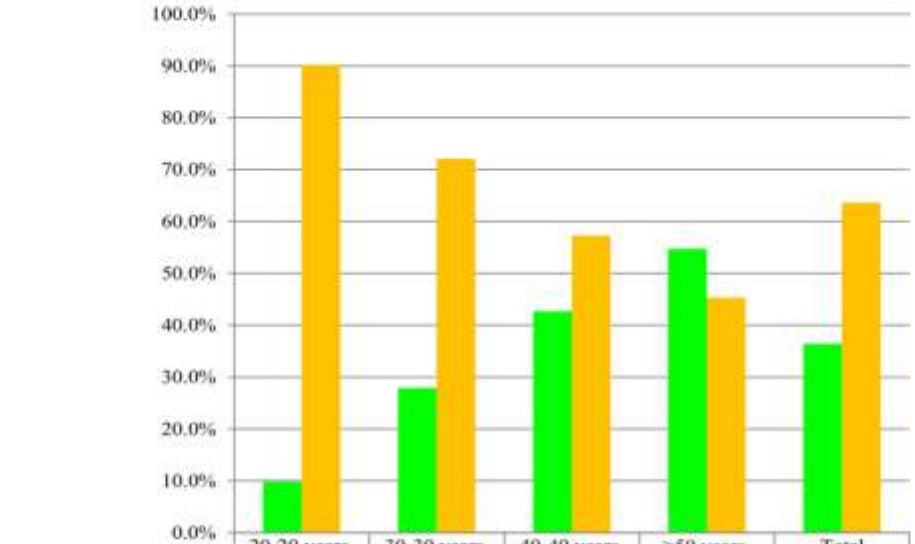


Figure 2. Patterns of metabolic syndrome among people with HIV on first-line treatment in relation to age categories.

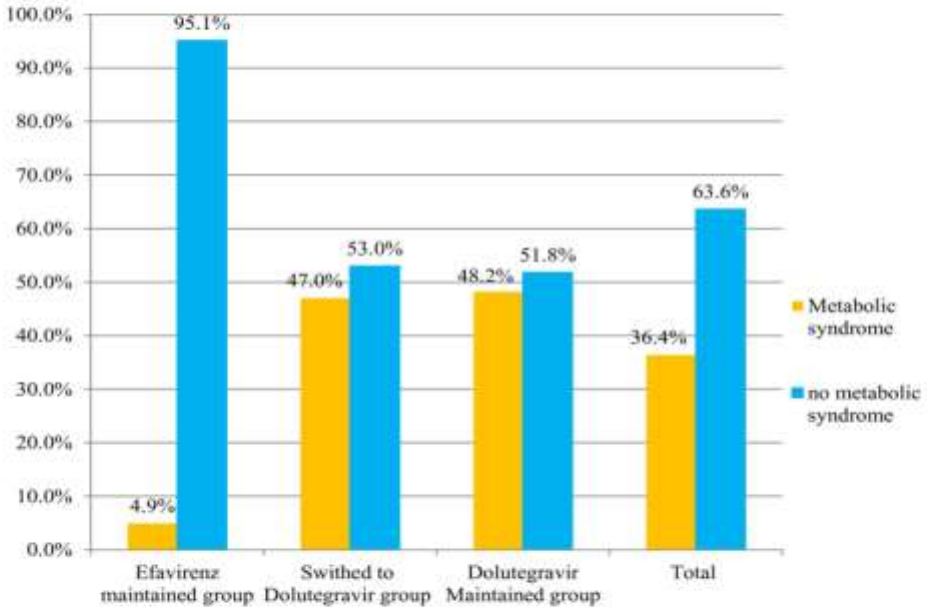


Figure 3. Patterns of metabolic syndrome among people with HIV on first-line treatment in relation to antiretroviral regimens.

Table 3. Prevalence of metabolic syndrome and its components among adult people living with HIV on first-line antiretroviral treatment.

Parameters	Total, 450 (%)	Females, 262 (%)	Males, 188 (%)	*p*-Value
Metabolic syndrome	164 (36.4)	91 (34.7)	73 (38.8)	0.373
Waist circumference (≥80 cm in women and ≥94 cm in men)	200 (44.4)	135 (51.5)	65 (34.6)	<0.001
Triglycerides (≥150 mg/dL)	154 (34.2)	72 (27.5)	82 (43.6)	<0.001
HDL-c (<50 mg/dL in women and <40 mg/dL in men)	368 (81.8)	234 (89.3)	134 (71.3)	<0.001
Fasting blood glucose (≥100 mg/dL)	110 (24.4)	59 (22.5)	51 (27.1)	0.262
Systolic and or diastolic blood pressure: (≥130/85 mmHg)	143 (31.8)	69 (26.3)	74 (39.4)	0.003
Body mass index (≥25 kg/m²)	202 (44.9)	131 (50)	71 (37.8)	0.01
Waist-hip ratio (≥0.85 in females and ≥0.9 in males)	280 (62.2)	150 (57.3)	130 (69.1)	0.01
Waist-height ratio (≥0.5)	293 (65.1)	184 (70.2)	109 (58)	0.007

HDL-c, high-density lipoprotein cholesterol.

cardiovascular health, and differences in the clinical and anthropometric characteristics of the populations.[44]

Low HDL-c was the most frequent component of MetS in this study, with a prevalence of 81.8%. Similarly, several studies have identified low HDL-c as the most frequently observed component of MetS among PLWH.[45,46] However, the finding was higher than the rates reported in previous studies, such as 64.1% in north-central Ethiopia,[47] 75% in young adults and 58% in adults in Zambia,[48] and 72.1% in Uganda.[19] Differences in treatment duration[19] and the varying effects of ART medications may also explain the observed variations in HDL-c level across studies.[49]

Sex was not associated with MetS in this study, which is consistent with reports from Nigeria[50] and Ethiopia.[51] In contrast, findings from apparently healthy general populations in Ethiopia[40,42] and several similar studies conducted in PLWH[14,36,52] have reported a significant association between female sex and MetS. This might be due to hormonal differences, abdominal fat distribution, level of physical activity engagement, and cultural factors, all of which differentially influence metabolic risk between sexes across studies.

In this study, more than 50% of participants over 50 years old had MetS, with older age being significantly associated with an increased risk of developing the condition. This finding was consistent with other studies conducted in Ethiopia.[40–42] In support, aging may contribute to the loss of muscle mass and strength due to reduced physical activity, leading to increased fat accumulation and decreased lean mass, which likely contribute to the development of MetS.[53]

A significant association between TG/HDL-c ratio and MetS was observed in this study, with each additional unit increase in TG/HDL-c corresponding to a 50% higher risk of developing MetS. The finding was consistent with previous studies that reported similar associations between TG/HDL-c and MetS,[54] further, highlighting its stronger association with the incidence of CVD.[55]

In this study, 62.4% of individuals with a BMI ≥25 kg/m² had MetS, and BMI was significantly associated with MetS. Similar findings have been reported in studies conducted both in Ethiopia and elsewhere.[12–15,36,43] In addition, this study found a significant association between WHtR and MetS, which is consistent with previous studies that reported similar findings.[54,56]

Table 4. Factors associated with metabolic syndrome among adults on first-line antiretroviral treatment.

Variable	Metabolic syndrome					
	Yes ($n=164$)	No ($n=286$)	cOR (95% CI)	*p*-Value	aOR (95% CI)	*p*-Value
Sex						
Males	73	115	1.00		1.00	
Females	91	171	0.8 (0.6–1.2)	0.373	1.8 (0.86–3.8)	0.116
Age						
≤50 Years old	122	253	1.00		1.00	
>50 Years old	42	33	2.6 (1.6–4.4)	<0.001	2.9 (1.4–6.2)	0.005
Alcohol intake status						
Never	49	139	1.00		1.00	
Former	69	105	1.8 (1.2–2.9)	0.006	1.4 (0.73–2.8)	0.293
Current	46	42	3.1 (1.8–5.3)	<0.001	2.7 (1.2–6.4)	0.019
Monthly income in ETB						
<4000 birr	70	183	1.00		1.00	
≥4000 birr	94	103	2.4 (1.6–3.5)	<0.001	1.2 (0.68–2.2)	0.507
Self-reported recalling problem						
No	107	211	1.00		1.00	
Yes	57	75	1.5 (0.99–2.3)	0.056	1.5 (0.82–2.7)	0.189
Family history of hypertension						
No/don't know	96	202	1.00		1.00	
Yes	68	84	1.7 (1.1–2.5)	0.009	2.1 (1.1–3.8)	0.023
Family history of diabetes						
No/Don't know	126	236	1.00		1.00	
Yes	38	50	1.4 (0.9–2.3)	0.144	0.8 (0.39–1.6)	0.523
Waist-hip ratio (≥0.85 in women and ≥0.9 in men)						
No	22	148	1.00		1.00	
Yes	142	138	6.9 (4.2–11.5)	<0.001	1.9 (0.95–3.9)	0.068
Waist-height ratio (≥0.5)						
No	10	147	1.00		1.00	
Yes	154	139	16.3 (8.2–32)	<0.001	5.4 (1.8–15.9)	0.002

(Continued)

Table 4. (Continued)

Variable	Metabolic syndrome					
	Yes (n = 164)	No (n = 286)	cOR (95% CI)	p-Value	aOR (95% CI)	p-Value
Physical exercise performance						
Moderate-high	88	216	1.00		1.00	
Inadequate	76	70	2.7 (1.8–4.0)	<0.001	1.7 (0.97–3.1)	0.063
Body mass index						
<25 kg/m²	38	210	1.00		1.00	
⩾25 kg/m²	126	76	9.2 (5.8–14.3)	<0.001	3.7 (1.9–7.1)	<0.001
TG/HDL-c ratio[a]	5.5 (3.5–8.7)	2.7 (2–3.6)	1.5 (1.4–1.7)	<0.001	1.5 (1.3–1.7)	<0.001
Treatment groups						
Efavirenz-maintained	8	9	1.00		1.00	
Switched to dolutegravir	77	127	07 (0.2–1.8)	0.45	0.62 (0.16–2.3)	0.482
Dolutegravir-maintained	79	150	0.6 (0.2–1.6)	0.30	0.52 (0.13–2.0)	0.340

[a]Continuous covariate.
aOR, adjusted odds ratio; ART, antiretroviral therapy; cOR, crude odds ratio; ETB, Ethiopian birr; HDL-c, High-density lipoprotein cholesterol; TG, triglyceride.

Our study also identified a significant association of MetS with a family history of hypertension, which is in line with previous research showing that individuals with such a family history are more likely to have obesity, central obesity, and MetS.[57] This may be due to inherited genetic traits that predispose individuals to elevated blood pressure and other metabolic abnormalities, thus increasing the risk of MetS.

We observed a significant association between alcohol consumption and MetS, which is consistent with results from other studies.[40,42,43] Alcohol may raise blood pressure and trigger metabolic changes linked to inflammation and obesity.[58,59] In PLWH, at-risk alcohol use exacerbates cardiometabolic and neurocognitive issues, which, combined with chronic ART use, contribute to frailty and age-related comorbidities.[60] Overall, these findings strongly support the link between alcohol use and accelerated biological aging, as well as an increased risk for comorbidities.[60]

Moreover, over 90% of participants with MetS were on DTG-based regimens in this study; however, no significant association was observed between DTG-based regimens and MetS. This finding is consistent with previous studies that reported similar results among individuals treated with DTG-based regimens.[61,62] In contrast, several other studies have reported a significantly higher incidence of treatment-emergent MetS among individuals on DTG-based regimens compared to those on non-DTG regimens,[17,52] with some also identifying a significant association between DTG and MetS.[63] The limited number of participants in the NNRTI group in our study, due to the national rollout of DTG treatment, may have contributed to the observed variation and influenced the interpretation of the association between DTG and MetS.

Strength and limitations of the study

A strength of our study is that it included all adults who initiated first-line ART across multiple health facilities following Ethiopia's adoption of a universal test-and-treat strategy. This strategy prioritizes a positive HIV diagnosis for ART initiation, regardless of CD4+ count or WHO clinical stage,

thus minimizing the inclusion of individuals with low CD4+ counts, advanced disease stages, or significant wasting syndrome, which could contribute to cardiometabolic complications. Additionally, the study included individuals who had undergone at most one switch within first-line regimens, reducing the potential for cardiometabolic complications associated with the use of multiple regimens or drugs. However, this study has several limitations. First, the cross-sectional design prevents establishing causal relationships between risk factors and MetS. Second, we did not conduct a nutritional assessment, despite its known association with MetS and cardiovascular risk. Third, the small number of participants on an NNRTI-based regimen may have limited our ability to fully interpret the association between ART regimens with MetS. Fourth, recall bias may have affected the accuracy of family history data, particularly regarding hypertension and diabetes, while reliance on self-reported data introduced potential bias and limitations in accuracy. Lastly, we used only the 2009 harmonized (JIS) criteria to assess MetS prevalence; different results may have been found if other criteria, such as WHO, NCEP-ATP III, or IDF, had been used.

Conclusion

We identified a high prevalence of MetS among adult PLWH in southern Ethiopia, with low HDL-c being the most frequently observed component. MetS was associated with both non-modifiable (age and family history of hypertension) and modifiable (BMI, WHtR, alcohol intake, and TG/HDL-c) risk factors, indicating a considerable cardiovascular risk. However, our study found no association between DTG-based first-line regimens and an increased risk of MetS.

Therefore, regular screening and monitoring for MetS components are essential to mitigate the health risks associated with metabolic abnormalities. As most of the identified risk factors are modifiable, effective lifestyle interventions are essential. In addition, implementing a comprehensive approach is essential for early diagnosis, preventing cardiovascular complications and enhancing incident management in this population. Furthermore, studies are required to investigate additional underlying factors and the long-term metabolic risks associated with ART.

Declarations

Ethics approval and consent to participate

This study was approved by the Institutional Review Board (IRB) of the College of Natural and Computational Sciences at Addis Ababa University, with ethical reference number IRB/07/14/2022. Participants were thoroughly informed about the study's objectives, potential risks, and the significance of the data being collected. Written informed consent was obtained from all participants in the study. For individuals unable to read or write, consent was obtained through legally authorized representatives, ensuring that the participant's rights and understanding of the study were upheld. Participation was entirely voluntary, and participants were made aware of their right to withdraw or decline at any stage without any consequences.

Consent for publication

Not applicable.

Author contributions

Agete Tadewos Hirigo: Conceptualization; Data curation; Formal analysis; Funding acquisition; Investigation; Methodology; Project administration; Resources; Software; Supervision; Validation; Visualization; Writing – original draft; Writing – review & editing.

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Zelalem Debebe: Conceptualization; Data curation; Formal analysis; Investigation; Methodology, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing.

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Availability of data and materials
The full dataset supporting this study is provided within the manuscript.

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Effects of lifestyle modification counselling on weight and body composition among adults with overweight or obesity on antiretroviral therapy: a randomized controlled trial

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ABSTRACT

Background: we aimed to evaluate the impact of lifestyle modification counselling on weight and body composition among adults with overweight or obesity receiving antiretroviral treatment (ART).
Methods: This randomized, open-label, controlled trial enrolled 126 adults aged 18–65 years, living with human immunodeficiency virus (HIV) and classified as overweight or obese. Of these, 116 participants (63 in the control group and 53 in the intervention group) completed the six-month follow-up. Weight and body composition outcomes were analyzed among those who completed the study, with comparisons made between baseline and post-intervention measurements. The effect of lifestyle modification counselling on weight and body composition was evaluated through linear mixed effects model and multiple linear regression analysis.
Results: Over the six-month trial, participants who received lifestyle modification counselling showed significantly greater reductions in body weight ($\Delta = -1.4$ kg, $p = 0.002$), visceral fat ($\Delta = -0.53$, $p = 0.006$), fat mass ($\Delta = -2.16$ kg, $p < 0.001$), and body fat percentage ($\Delta = -2.02$ %, $p < 0.001$) compared to the control group. The intervention group experienced greater increases in fat-free mass ($\Delta = +0.673$ kg, $p = 0.068$) and percentage skeletal muscle ($\Delta = +1.27$ %, $p < 0.001$) compared to the control group. Additionally, lifestyle modification counselling significantly contributed to achieving at least a 3 % weight loss from baseline ($\beta = 0.158$, $p = 0.048$).
Conclusion: Lifestyle modification counselling resulted in promising and favorable changes in weight and body composition. Therefore, offering routine structured counselling interventions within ART clinics for individuals with overweight or obesity may help reduce obesity-related health risks and improve clinical outcomes (Thai Clinical Trials Registry TCTR20240905007).

1. Introduction

Individuals living with human immunodeficiency virus (HIV) who are receiving antiretroviral treatment (ART) are more likely to experience obesity compared to the general population [1]. The weight gain observed in this group might be influenced by a variety of factors, which include the obesogenic situation, metabolic as well as immune changes associated with HIV, specific ART regimens and demographic variables [2]. Excess weight gain in people living with HIV (PLWH) is associated with an elevated risk of noncommunicable diseases (NCDs), which occur more frequently in this population compared to those without HIV [3,4]. Additionally, obesity in PLWH is considered as a risk factor for cardiovascular and metabolic disorders and certain cancers [5,6].

Recent studies have highlighted differential degrees of weight gain associated with various ART medications [7,8]. Integrase strand transfer inhibitors (INSTIs), particularly dolutegravir (DTG)-based regimens, are

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highly recommended by the World Health Organization (WHO) and widely used in Sub-Saharan Africa (SSA) due to their effectiveness, low resistance and safety [9]. Despite their established efficacy, DTG-based regimens have been associated with undesirable effects, including potential cardiometabolic risks [7,10]. In addition, emerging evidence suggests an increased risk of weight gain with these regimens [11,12] and prior findings from this study project showed that 50 % of participants initiating first-line ART gained ≥10 % of their baseline weight within 24-months [13]. A significant proportion of those who gained excess weight were on DTG-based therapies [13]. As a result, various studies have recommended the implementation of weight-loss interventions for PLWH on INSTIs-based regimens [14–16].

Studies have emphasized the importance of behavioral interventions, particularly dietary changes and regular physical activity as primary and non-pharmacological options for weight loss and managinig obesity-related conditions [17,18]. Robust evidence suggests that interventions combining caloric restriction with exercise can effectively facilitate healthy weight loss, leading to decreases in both subcutaneous and visceral fat among PLWH [19–21]. Importantly even modest reductions in weight can yield substantial long-term health advantages for adults with obesity in the general population [22,23], including cardiometabolic risk profiles [17]. Consequently, implementing lifestyle changes focused on weight reduction is crucial for individuals with overweight and or obesity, considering the substantial health risks that obesity poses to this group [24,25]. Regular lifestyle counselling represents an essential and cost-effective method to support healthy weight loss, sustainable management management and cardiovascular risk risk reduction in this population [71].

Although Ethiopia has began integrating NCD care into HIV services but lifestyle modification counselling is not consistently provided to PLWH who are overweight or obese and receiving ART. The increasing prevalence of weight gain associated with newer ART treatments, exacerbated by sedentary lifestyles and limited engagement in health-promoting activities, underscores the urgent need for wellcontrolled studies. This study aimed to assess the impact of lifestyle modification counselling on weight and body composition among adult PLWH with a body mass index (BMI) ≥25 kg/m^2 who were receiving first-line ART. Using a randomized trial design, the study aimed to highlight the effectiveness of these interventions and their relevance to HIV care.

2. Materials and methods

2.1. Study setting

This study was done in Hawassa city in Sidama Region, southern-Ethiopia, located 275 km from Addis Ababa. Hawassa city covers an area of 157.2 km^2, is divided into 8 sub-cities and consists of 32 kebeles (the smallest administrative unit or neighbourhood within a district or sub-city). According to the 2022 report from the City Administration Health Department, the city had an estimated population of 402,903, comprising 201,532 males and 201,371 females. The city administration was providing ART services to over 6300 PLWH through eight health facilities during the study period.

2.2. Study design and participants

This randomized, open-label, controlled trial (Thai Clinical Trials Registry TCTR20240905007) investigated the effects of behavioral lifestyle interventions in adults with overweight or obesity receiving ART. Randomization was performed using a simple lottery method based on the participants' arrival for routine ART follow-up visits. Participants were sequentially assigned to either the intervention or the control group, ensuring comparable age distribution across groups. The intervention group received personalized face-to-face counselling on behavioral lifestyle changes at baseline, followed by at least two phone-counselling sessions within two months to encourage adherence. In contrast, the control group received routine care from the ART clinics. Both study groups underwent baseline data collection prior to the intervention and were followed up for six months after the initial face-to-face counselling session.

To be eligible, PLWH had to have a BMI ≥25 kg/m^2, be aged 18–65 years, and have been on first-line ART for at least 12 months following Ethiopia's test-and-treat strategy. Additionally, eligible participants had a baseline physical activity level below 600 metabolic equivalents of task per week (MET-min/week) and were free from opportunistic infections during the study period. Importantly, none had previously received formal dietary or physical activity counselling or participated in structured nutrition or physical activity programs.

Additionally, participants were required to have achieved viral suppression, defined as an HIV ribonucleic acid (RNA) viral load below 1000 copies/mL, and demonstrated at least fair adherence to ART (missing no more than 3–4 doses out of 30 or 4–9 doses out of 60) [26]. All participants provided written informed consent prior to enrolment. Their first-line ART regimen included two nucleoside/nucleotide reverse transcriptase inhibitors plus either efavirenz- or dolutegravir-based combinations.

Exclusion criteria included a history of pulmonary or cardiac complications, neurological or musculoskeletal disorders, diagnosed thyroid disease, uncontrolled hypertension, or any physical condition that limited participation in physical activity. Pregnant women, those with chronic liver or renal disease, and participants who had begun Ethiopian Orthodox Christian Lent and Ramadan fasting practices during the study period were also excluded. Study enrolment took place between January 5, 2023, and May 30, 2024.

2.3. Sample size determination

For this trial study, the OpenEpi 3.01 software was used to estimate sample size, with the focus on changes in body weight following lifestyle modification counselling. The calculation was based on a 95 % confidence interval (CI) and 80 % power. At the three-month assessment, the counselled group had a mean 85.6 kg (±15.96) weight, with mean 4.09 kg reduction from baseline [27]. While, the participants in control arm had an average weight of 94.02 kg (±14.96), indicating a mean 0.65 kg increase from baseline [27]. Initially, the sample size was calculated to be 106, but it was adjusted to 132 to account for a 20 % attrition rate. As a result, 66 participants were randomly assigned to each group, with randomization based on their arrival according to the ART clinic's follow-up schedule.

2.4. Intervention

The goal of the lifestyle modification intervention was to achieve and maintain at least a 3 % reduction in weight from baseline through individualized counselling, including an initial face-to-face session followed by a minimum of two phone-based remote counselling sessions. The intervention included specific strategies such as modifying dietary intake habit, caloric restriction and increasing body exercise (performing at least moderate-intensity physical activity). Trained counsellor (ART clinic nurse) conducted counselling. The training materials for counsellor were developed by adapting guidelines and literature on body weight management, emphasizing the importance of healthy weight reduction [28–33]. The initial session was an individual based face-to-face contact, lasting 50–60 min, with a focus on promoting lifestyle changes. All intervention components were explained in Amharic language during counselling supported by pictures and photographs during face-to-face interviews and discussions. Each participant received nutrition counselling from a trained counsellor, who utilized motivational interviewing techniques overseen by the principal investigator. During the counselling sessions, counsellor encouraged participants' lifestyle modifications to reduce caloric intake of at least 500 kcal/day. To achieve this they were advised to use strategies such as

reducing portion sizes, limiting high-calorie foods (e.g., fried foods, sugary drinks), choosing low-energy-dense foods like vegetables and whole grains, and promoting regular meal patterns, lean protein and low fat and oils into their daily diets. In addition, they recommended incorporating locally available fibre-rich foods, like whole grains, green vegetables, Moringa *oleifera* leaves, and fruits into their diets. They also advised avoiding overeating and to reduce or eliminate the intake of refined grains, fats particularly saturated types, added sugars, high-calorie foods, fast foods and sugary or processed foods.

Regarding exercise, all participants in the intervention group were encouraged to engage in at least 150 min of moderate-intensity exercise per week, primarily consisting of aerobic activities. In addition to this, they were advised to perform physical exercises in line with the program aired on Ethiopian television, either choosing morning or evening sessions based on their preference. They were also highly advised to minimize sedentary behaviours, including prolonged sitting, watching television, using a computer, or playing video games [34,35]. Each participant in the intervention group received a brochure, written in Amharic language, which was adapted from multiple guidelines and previously published literature on body weight management [28–33]. This brochure included both narrative text and pictorial illustrations offering guidance on dietary modifications, behavioural changes, and the promotion of physical activity to support effective weight loss. Furthermore, participants received at least two remote counselling sessions via phone calls, each lasting 20–30 min within the first two months following randomization, to support and encourage them to adhere to the recommended lifestyle changes. In contrast, the control group have not received lifestyle modification counselling throughout the study but they were asked to visit and attend the final assessment. Apart from the counselling, participants received the routine care from the ART clinics service. Following the final assessment, they were provided with lifestyle modification counselling to enable them to achieve the anticipated benefits.

2.5. Data collection

Data on sociodemographic and socioeconomic factors, behavioral characteristics, clinical information, food frequency and 24-h dietary recall (24HR) were collected through a questionnaire written in the Amharic language administered by an interviewer. All data were gathered in isolated rooms according to the measurement protocol. To capture detailed information on all foods and beverages consumed by participants, a structured 24HR questionnaire was used. This covered everything consumed within 24 h, typically from morning of the previous day to the morning of the next day.

To estimate food intake, standard measuring tools, common-size containers and pictorial displays of food items were used. Photographs illustrating different portion sizes was used to facilitate precise estimation of the foods consumed and their respective portion sizes according to the participants' responses. This process enabled the calculation of average daily use of total calorie, macronutrients (carbohydrates, proteins and fats) and fibre amount. These estimates were computed using Ethiopian Food Composition Tables and Ethiopian Food-Based Dietary Guidelines [36–38]. A questionnaire on dietary diversity and food frequency was used to evaluate the participants' usual food intake. The number of distinct food groups consumed by participants over the past 24 h was used to determine the Individual Dietary Diversity Score (IDDS). For this assessment, food items were categorized into ten specific groups. A DDS of less than 5 indicated low dietary diversity, while a score of 5 or more reflected diversified food consumption [39,40]. In addition, the baseline physical exercise status of each individual was evaluated using the short form of the International Physical Activity Questionnaire [41,42].

2.6. Outcome measurement and assessments

The outcome variables were measured at baseline, before the initiation of counselling, and again at the end of the six-month intervention. Measurements of body height done by a Seca stadiometer from Germany, while waist circumference and hip circumference were measured with non-elastic measuring tape and recorded in centimetres (cm). Body weight in kilogram, BMI (kg/m^2) and body composition including body fat percentage (BFP), visceral fat (rated on a scale of 1–30) and percentage of skeletal muscle were obtained through bioelectrical impedance analysis using the Omron Full Body Sensor Body Composition Monitor and Scale (Omron HBF–514C: Omron Healthcare Ltd.) [43], and measured as per manufacturers protocol. Fat mass (FM) was calculated by multiplying body weight by the BFP divided by 100, while fat-free mass (FFM) was determined by subtracting FM from total body weight, using the formula: FFM = weight − [weight × (BFP/100)]. The Fat Mass Index (FMI) is calculated by dividing FM by the square of height (m^2), expressed as: FMI = FM (kg)/height (m^2). Similarly, the Fat-Free Mass Index (FFMI) is determined by dividing FFM by the square of height (m^2), represented as: **FFMI = FFM (kg)/height (m^2).**

To ensure data accuracy, each outcome variable was measured twice for every participant at each phase and the mean of these values was recorded and used for analysis. The same counsellor provided the intervention consistently throughout the study to reduce interpersonal bias and body weight measuring instrument was calibrated daily with standard calibration tools.

The primary outcomes were changes in weight and body composition, measured at baseline and after six months. The the study also aimed to achieve at least a 3 % reduction in weight from baseline after six months of lifestyle modification counselling. This weight loss was expressed as a percentage change from baseline for each participant, using the formula: [(value at 6 months − value at baseline)/value at baseline] × 100.

2.7. Statistical analysis

To minimize biases from non-completers, we conducted a per-protocol analysis, comparing study groups based only on participants who completed the study as planned. Descriptive statistics were employed to summarize the study variables. Categorical variables are presented as frequencies and percentages, while numerical variables are reported as means with standard deviations (SD) or as medians with interquartile ranges (IQRs). The χ^2 test was applied to evaluate the demographic characteristics of the participants and Independent *t*-test was used to compare baseline characteristics between the study groups. A paired *t*-test was used to calculate within-group changes in quantitative variables from baseline. An independent *t*-test was used to evaluate the differences in scores between the pre-test and post-test results for both the intervention and control groups. Demographic variables and weight loss were dummy coded before analysis. Multicollinearity was evaluated using the variance inflation factor (VIF), with values < 10 considered acceptable for this analysis. Linear regression, adjusted for baseline values was employed to assess changes in weight and body composition, as well as to determine a weight loss of at least 3 %. A linear mixed-effects model was also employed to assess the effect of counselling on weight and body composition variables over time. Statistical significance was determined at a 5 % alpha level with a 95 % CI. Analyses were performed using SPSS version 27.0 and STATA version 17.0.

3. Results

3.1. Participants' baseline characteristics

Overall, 126 adults with overweight and obesity were randomly allocated into two groups, each consisting of 63 individuals. Following randomization, 10 participants were excluded from the intervention

group due to failure to complete the study (Fig. 1). Table 1 indicates the study completed participants' baseline characteristics (n = 116). There were no statistically significant differences between these groups in baseline variables (all $p > 0.05$), except for dietary fibre consumption level. For both study groups, the average age was 43.6 years (SD ± 8.6), and the average BMI was 29.7 kg/m^2 (SD ± 4.8). The majority were females (71/116, 61.2 %) and overweight (79/116, 68.1 %). Regarding ART regimens, more than 95 % in each group were on DTG based first line regimens.

3.2. Baseline dietary diversity score and food frequency patterns of the study participants

Average DDS among the study participants was 4.1 (±0.97). A substantial proportion, 72.4 %, displayed low dietary diversity, with 4.3 % consuming foods from only two groups, 19.8 % from three groups and 48.3 % from four groups. In contrast, 27.6 % of participants included foods from five or more food groups in their diet. An adequate DDS is characterized by the intake of ≥5 diverse food groups. It was achieved by 26.4 % of participants in the intervention group and 28.6 % in the control group.

In terms of food frequency, over 98 % of participants reported consuming foods made from cereals, grains, and white roots or tubers more than once a day. In comparison, only 3.4 % of participants ate fruits daily, while 14.7 % consumed vegetables on a daily basis. Fish was the least frequently consumed food, with only 0.9 % of participants eating it once per week (Table 2).

3.3. Changes after six-month intervention

Table 3 presents the intragroup comparisons of variables after six months. Intervention group showed average 0.6 kg (95 %CI -1.3, 0.11; p = 0.11) weight loss from their baseline, whereas control participants gained 0.8 kg (95 %CI 0.27, 1.3; p = 0.004) weight from their baseline. WC and HC in the intervention group showed significant reductions from their baseline ($p < 0.05$). Significant change in BFP, FM and FMI was observed in the counselled group: BFP decreased by 1.4 % (95 %CI -2.0, −0.86, $p < 0.001$), FM by 1.38 kg (95 %CI -2.1, −0.6, p = 0.001) and FMI by 0.54 kg/m^2 (95 %CI -0.85, −0.24, p = 0.001) from baseline. In contrast, the controls showed significant increases in BFP (+0.6 % [95 % CI 0.12, 1.1, p = 0.01]), FM (+0.78 kg [95 %CI 0.27, 1.3, p = 0.003]), FMI (+0.3 kg/m^2 [95 %CI 0.1, 0.5, p = 0.004]) and visceral fat (+0.28 [95 %CI 0.09, 0.48, p = 0.005]) from their baseline.

The intergroup comparison of differences over six months revealed significant changes among participants in the intervention group compared to the controls. Participants in the counselling group lost

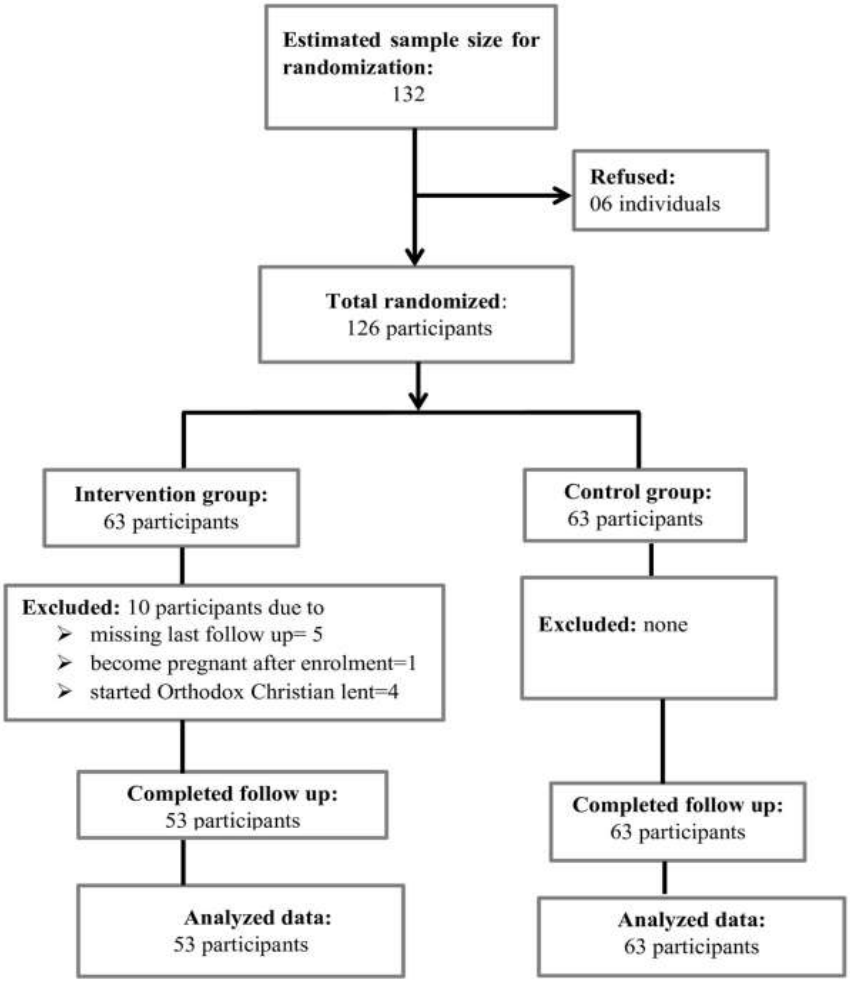


Fig. 1. Flowchart depicting the study participants' inclusion process.

Table 1
Baseline general characteristics of the study participants.

Variables	Category	Total n = 116	Study groups		p value
			Intervention n = 53	Controls N = 63	
Sex	Females	71 (61.2)	32 (60.4)	39 (61.9)	0.866[a]
	Males	45 (38.8)	21 (39.6)	24 (38.1)	
Age, years	Mean (SD)	43.6 (8.7)	42.8 (7.0)	44.3 (9.9)	0.347[b]
ART duration, years	Mean (SD)	4 (1.8)	3.78 (1.8)	4.1 (1.8)	0.289 [b]
Height, centimetre	Mean (SD)	1.6 (0.1)	1.6 (0.09)	1.6 (1.1)	0.373 [b]
Weight	Mean (SD)	76.8 (11.9)	79 (11.4)	75 (12.1)	0.071 [b]
Body mass index, kg/m^2	Mean (SD)	29.4 (4.4)	29.7 (4.8)	29.0 (4.1)	0.397 [b]
	25–29.9 kg/m^2	79 (68.1)	35 (66.0)	44 (69.8)	0.662[a]
	≥30 kg/m^2	37 (31.9)	18 (34.0)	19 (30.2)	
WC, centimetre	Mean (SD)	97 (9.2)	97.7 (9.6)	96.4 (8.9)	0.462 [b]
Hip circumference	Mean (SD)	103.9 (8.8)	105.1 (10)	102.9 (7.5)	0.175 [b]
Waist-hip ratio	Mean (SD)	0.94 (0.097)	0.93 (0.098)	0.94 (0.096)	0.715 [b]
HDL-cholesterol	Mean (SD)	36.4 (8.3)	35.9 (7.5)	36.7 (9)	0.61[b]
Percent body fat	Mean (SD)	39.7 (4.9)	40.6 (9.6)	39.1 (7.8)	0.364 [b]
Fat mass index, kg/m^2	Mean (SD)	11.8 (3.9)	12.39 (4.7)	11.29 (3.0)	0.130 [b]
VF level (1–30 range)	Mean (SD)	9.97 (2.96)	9.9 (2.5)	10 (3.3)	0.821 [b]
Fat free mass, kg	Mean (SD)	46.3 (10)	46.7 (8.8)	45.98 (11)	0.698 [b]
Fat free mass index, kg/m^2	Mean (SD)	17.3 (2.0)	17.36 (1.9)	17.32 (2.1)	0.928 [b]
Percent skeletal muscle	Mean (SD)	26.2 (4.9)	26 (5.3)	26.3 (4.6)	0.791 [b]
Total energy, Kilocalorie	Mean (SD)	2034 (435.3)	2008.7 (398.6)	2056 (466)	0.563 [b]
Carbohydrate, Kilocalorie	Mean (SD)	1417.3 (306.4)	1371.5 (259.2)	1456 (338.4)	0.14 [b]
Protein, Kilocalorie	Median (IQR)	211.5 (177–299)	194.6 (169–324)	211 (185–274)	0.673[c]
Fat, Kilocalorie	Median (IQR)	336.4 (238–465)	342 (249.5–485)	323 (230–451)	0.576[c]
Fibres, grams	Mean (SD)	32.8 (13.5)	29.4 (12.7)	35.7 (13.7)	0.012 [b]

Values are presented as numbers (%) unless otherwise indicated; ART, antiretroviral therapy; HDL, high density lipoprotein; WC, waist circumference; VF, visceral fat; IQR: interquartile range; kg, kilogram; m^2, square meter; SD, standard deviation; ([a], significance by chi square test; [b], significance by independent *t*-test; [C], significance by Mann-Whitney U tests).

Table 2
Food frequency patterns of the study participants (n = 116).

Frequency of food item intake	Grains, roots and Tubers (%)	Pulses (%)	Seeds and nuts (%)	Eggs (%)	Dairy products (%)	Meat and meat products (%)	Any vegetables (%)	Any fruits (%)	Fats and oils (%)	Fishes (%)	Sweets and drinks (%)
Never	0.0	0	48.3	52.6	49.1	48.3	8.6	19	0.0	99.1	69.8
Once/week	0.0	0.9	25.9	19.8	8.6	12.9	14.7	16.4	0.0	0.9	0.9
Two times/week	0.0	2.6	13.8	16.4	13.8	23.3	25.9	35.3	0.0	0.0	11.2
3-4 times/week	0.0	1.7	8.6	6.0	10.3	10.3	35.3	21.6	0.0	0.0	4.3
5-6 times/week	0.0	0.9	1.7	0.0	0.9	1.7	8.6	4.3	0.0	0.0	1.7
Once/day	1.7	6.9	0.9	5.2	12.9	3.4	14.7	3.4	0.0	0.0	10.3
>1 times/day	98.3	87.1	0.9	0.0	4.3	0.0	0.9	0.0	99.1	0	1.7
Total (%)	100	100	100	100	100	100	100	100	100	100	100

Table 3
Changes in body composition and blood pressure from baseline to six-month intervention.

Outcome variables	Changes within group[a]					
	Intervention group (n = 53)			Control group (n = 63)		
	At 6 month Mean (SD)	Δ from baseline Mean (95 %CI)	p-value	At 6 month Mean (SD)	Δ from baseline Mean (95 %CI)	p-value
Weight, kg	78.5 (11.7)	−0.6 (-1.3, 0.11)	0.10	75.98 (11.97)	+0.8 (0.27, 1.3)	0.004
Body mass index, kg/m^2	29.53 (4.8)	−0.23 (-0.49, 0.03)	0.078	29 (2.9)	−0.048 (-0.09, 0.8)	0.94
Waist circumference, cm	96.35 (9.6)	−1.3 (-2.2, −0.45)	0.004	95.87 (8.9)	−0.53 (-1.2, 0.15)	0.13
Hip circumference, cm	103.46 (9.9)	−1.7 (-2.4, −0.9)	<0.0001	102.11 (7.4)	−0.79 (-1.5, −0.1)	0.02
%Body fat	39.02 (9.3)	−1.4 (-2.0, −0.86)	<0.0001	39.66 (7.6)	+0.6 (0.12, 1.1)	0.01
Fat mass, kg	30.95 (10)	−1.38 (-2.1, −0.6)	0.001	29.83 (6.2)	+0.78 (0.27, 1.3)	0.003
Fat mass index, kg/m^2	11.8 (4.6)	−0.54 (-0.85, −0.24)	0.001	11.59 (2.97)	+0.3 (0.1, 0.5)	0.004
Visceral fat (1–30 range)	9.66 (2.5)	−0.24 (-0.59, 0.1)	0.15	10.32 (3.3)	+0.28 (0.09, 0.48)	0.005
Fat free mass, kg	47.5 (8.5)	+0.84 (0.18, 1.5)	0.014	46.15 (10.9)	+0.17 (-0.2, 0.5)	0.37
Fat free mass index, kg/m^2	17.69 (1.9)	+0.34 (0.08, 0.6)	0.01	17.39 (2.0)	+0.06 (-0.08, 0.2)	0.38
% Skeletal muscle	26.77 (5.1)	+0.9 (0.51, 1.31)	<0.0001	25.92 (4.4)	−0.34 (-0.8, 0.06)	0.096
Systolic BP(mmHg)	125 (17.7)	−3.1 (-6.3, 0.2)	0.065	124.3 (21.7)	−1.4 (-4.9, 2.2)	0.44
Diastolic BP(mmHg)	81.2 (10.9)	−3.7 (-6.2, −1.2)	0.004	80.2 (13.1)	−1.4 (-4.6, 1.8)	0.39

BP,blood pressure; CI, confidence interval; cm, centimetre; mmHg, millimetre of mercury; SD, standard deviation.
[a] Changes in variables within group was assessed by paired *t*-test.

substantial weight (−1.4 kg [95 %CI -2.2, −0.53]), BFP (−2.02 % [95 % CI -2.7, −1.3]), FM (−2.16 kg [95 %CI -3.1, −1.3]), FMI (−0.847 kg/m^2 [95 % CI -1.2, −0.495]), and VF (−0.53 [95 % CI -0.904, −0.157]) compared to controls at 6 months. In addition, the counselled group showed greater improvement in percentage skeletal muscle mass than controls (+1.27 % [95 %CI: 0.68, 1.8]). Cohen's d values for differences were indicated as follows: for weight, d = −0.6 (medium effect); for BFP, d = −1.03 (large effect); for FM, d = −0.889 (large effect); for VF, d = −0.525 (medium effect); and for percentage skeletal muscle mass, d = 0.8 (large effect) (Table 4).

3.4. Correlations between counselling and changes in weight and body composition

Counselling was significantly correlated with reduction in weight, resulting in a mean weight loss of 1.43 kg (β = −1.43, 95 % CI: 2.4, −0.45). Counselling also was correlated with an average decrease of 1.76 % in BFP (β = − 1.76, 95 % CI: 2.5, − 0.97) and an increase of 1.28 % in percentage skeletal muscle mass (β = 1.28, 95 % CI: 0.67, 1.9), suggesting a a favourable effect on muscle composition (Table 5).

After adjusting for covariates, significant interaction effects of "group × time" was found for variables such as weight (β = −1.1, 95 %CI -1.9, −0.3, p = 0.006), BFP (β = −1.8, 95 %CI -2.5, −1.1, p < 0.0001), FFM (β = 0.7, 95 %CI 0.18, 1.2, p = 0.009), and percentage skeletal muscle mass (β = 1.2, 95 %CI 0.63, 1.8, p < 0.0001).

Overall, 33.6 % of participants showed a reduction of ≥1 % of their baseline weight, with 43.4 % in the intervention group and 25.4 % in the control group (p = 0.041). In addition, 18.1 % lost at least 3 % of their body weight from baseline. Of these, 24.5 % participants were from the intervention group and 12.7 % were from controls. Multiple linear regression analysis showed that counselling had a significant effect on achieving at least a 3 % reduction in weight from baseline (Table 6).

Table 4
Effect size of intervention on anthropometrics, body composition and blood pressure.

Between group difference (Intervention group Vs. Controls).[a]			
Outcome variables	Δ from Control	Significance	Effect size
	Mean (95 %CI)	p-value	Cohen's d (95 % CI)
Weight, kg	−1.4 (-2.2, −0.53)	0.002	−0.6 (-0.973, −0.266)
Body mass index, kg/m^2	−0.18 (-1.7, 0.80)	0.71	−0.068 (-0.43, 0.297)
Waist circumference, cm	−0.8 (-1.9, 0.29)	0.148	0.271 (-0.638, 0.096)
Hip circumference, cm	−0.876 (-1.9, 0.13)	0.087	−0.322 (-0.689, 0.047)
Body fat (%)	−2.02 (-2.7, −1.3)	<0.0001	−1.03 (-1.42, −0.642)
Fat mass, kg	−2.16 (-3.1, −1.3)	<0.0001	−0.887 (-0.127, −0.503)
Fat mass index, kg/m^2	−0.847 (-1.2, −0.495)	<0.0001	−0.887 (-1.27, −0.502)
Visceral fat (1–30 range)	−0.53 (-0.904, −0.157)	0.006	−0.525 (-0.895, −0.152)
Fat free mass, kg	+0.673 (-0.05, 1.39)	0.068	0.34 (-0.025, 0.711)
Fat free mass index, kg/m^2	+0.27 (-0.007, 0.55)	0.056	0.36 (-0.009, 0.728)
Skeletal muscle (%)	+1.27 (0.68, 1.8)	<0.0001	0.80 (0.42, 1.18)
Systolic BP(mmHg)	−1.7 (-6.5, 3.1)	0.49	−0.129 (-0.494, 0.237)
Diastolic BP(mmHg)	−2.3 (-6.5, 1.8)	0.267	−0.21 (-0.574, 0.159)

BP,blood pressure; CI, confidence interval; cm, centimetre; kg, kilogram; mmHg, millimetre of mercury.

[a] Change score in variables between groups assessed by independent *t*-test; Effects size based on Cohen's d: <0.19 for insignificant; 0.20–0.49 for small; 0.50–0.79 moderate and >0.80 for large.

4. Discussion

This study assessed the impacts of counselling on weight and body composition variables. The counselling included one in-person session at randomization, followed by at least two telephone sessions within two months of intervention. Over six months, participants in the counselling group led to substantial decrease in weight (−1.4 kg), BFP (−2.0 %) and FM (−2.16 kg) compared to the controls. Additionally, considerable increase in percentage skeletal muscle (+1.27 %) and FFM (+0.67 kg) were observed among participants in the counselling group when compared to controls. Lifestyle modification counselling was also showed significantly correlation with achieving a minimum weight loss of 3 %.

Participants who received counselling experienced a significant decrease in weight (−1.4 kg) over six months compared to the control group. The finding is consistent with previous studies showing similar results with face-to-face, remote or combined counselling interventions [44–47]. Additionally, meta-analysis studies have demonstrated that increased counselling intensity significantly improves weight loss outcomes [48,49].

Studies have shown that lifestyle interventions combining dietary modifications and regular physical activity are effective for weight loss and obesity management [18,50]. However, the intragroup comparison in our counselling group indicated small weight loss from baseline, contrary to reports of other studies [51,52]. This may be attributed to the considerable increase in FFM and percentage skeletal muscle in our study, which may have replaced weight loss and influenced the weight loss results.

We found significant reductions in BFP (−1.4 %) and FM (−1.38 kg) in the counselled group from their baseline. Additionally, the intervention group showed significant reductions in BFP (−2.0 %), VF (−0.53), and FM (−2.16 kg) compared to the control group. These results are consistent with findings from several studies conducted among individuals with chronic health conditions, the general population [53–55], and PLWH [56,57].

PLWH on ART may be at increased risk of subcutaneous and visceral fat accumulation, contributing to central obesity and potentially increasing the risk of certain cancers through metabolic and inflammatory pathways [58], as well as elevating metabolic and cardiovascular risks [59]. Therefore, non-pharmacological treatments such as lifestyle interventions are essential for promoting healthy weight loss and reducing the impact of obesity among individuals with obesity [17,18]. Additionally, we observed a significant increase in FM (+0.78 kg) and VF levels (+0.28) in the control group from their baseline. This finding aligns with previous studies that reported similar results [60]. Inadequate physical exercise in PLWH compared to those without HIV, may contribute to alterations in body composition including the accumulation of central fat [61].

Studies have shown improvements in skeletal muscle mass, with a significant increase in the intervention group compared to the controls [62–64]. Consistent with these findings, we observed a substantial increase in percentage skeletal muscle in the counselled group from their baseline (+0.91) and compared to the control group (+1.27). Dietary modifications [65], along with increased exercise among participants in the counselling group may have contributed to this improvement in skeletal muscle [63,65].

In this study, participants in the counselling group showed a significant increase in FFM over six months from baseline; however, this increase was not significantly different from that in the control group. These findings are consistent with previous studies reporting increases in FFM among individuals with overweight or obesity who received lifestyle interventions [49,66]. Improvements in physical activity and dietary habits following counselling may promote the progress of skeletal muscle and increases in FFM [67].

Table 5
Linear regression model for associations of intervention with changes in weight and body composition.

Baseline variables	Body weight (Δ)		%body fat (Δ)		%skeletal muscle (Δ)	
	β(95 % CI)	P-value	β(95 % CI)	P-value	β(95 % CI)	P-value
Constant	2.4 (-4.3, 9.1)	0.481	5.8 (0.39, 11.2)	0.036	−0.26 (-3.9, 3.4)	0.887
Intervention	−1.43 (-2.4, −0.45)	0.005	−1.76 (-2.5, −0.97)	<0.0001	1.28 (0.67, 1.9)	<0.0001
Baseline weight	−0.006 (-0.05,0.03)	0.767	−0.02 (-0.05, 0.016)	0.703	−0.003 (-0.03, 0.02)	0.80
Age	−0.01 (-0.07, 0.05)	0.725	−0.028 (-0.08, 0.02)	0.318	0.03 (-0.08, 0.07)	0.123
Alcohol intake	0.15 (-0.12, 0.93)	0.779	−0.06 (-0.93, 0.81)	0.757	−0.05 (-0.72, 0.63)	0.893
ART duration	0.07 (-0.19, 0.34)	0.578	0.03 (-0.19, 0.24)	0.80	−0.07 (-0.24, 0.09)	0.393
DTG-based regimen	1.1 (-1.2, 3.4)	0.338	−0.54 (-2.4, 1.36)	0.569	0.45 (-0.99, 1.9)	0.538
Baseline Carbs calorie	−0.001 (-0.003, 0.00)	0.148	0.0 (-0.002, 0.001)	0.867	0.001 (-0.001, 0.002)	0.322
Baseline Protein calorie	0.00 (-0.003, 0.004)	0.780	−0.001 (-0.004, 0.002)	0.457	*	–
Baseline Fat calorie	0.003 (0.0, 0.007)	0.086	0.2 (-0.69, 1.1)	0.659	0.001 (-0.001, 0.004)	0.222
Baseline fibers intake	0.018 (-0.03, 0.06)	0.418	0.01 (-0.02, 0.05)	0.539	−0.014 (-0.04, 0.01)	0.298
Baseline dietary diversity	−0.5 (-1.6, 0.63)	0.393	0.18 (-0.70, 1.06)	0.686	0.24 (-0.44, 0.92)	0.484
Baseline %body fat	−0.02 (-0.08, 0.04)	0.437	−0.05 (-0.1, −0.005)	0.031	*	–
Baseline % skeletal muscle	*	–	*	–	−0.08 (-0.24, −0.02)	0.013
Baseline systolic BP	0.006 (-0.03, 0.04)	0.731	0.03 (0.007, 0.06)	0.016	−0.02 (-0.04, −0.001)	0.044
Baseline diastolic BP	−0.017 (-0.07, 0.03)	0.513	−0.06 (-0.1, −0.017)	0.006	0.04 (0.008, 0.07)	0.014
Baseline triglyceride level	0.001 (-0.005, 0.007)	0.696	0.003 (-0.002, 0.008)	0.2183	−0.004 (-0.008, −0.001)	0.027

Δ, change from baseline; DTG, dolutegravir; variance inflation factor for body weight = 8.7; % body fat = 8.7 % skeletal mass = 8.6; * excluded variable with a variance inflation factor of ≥10.

Table 6
Association of interventions with ≥3 % weight loss among the study participants.

Variables	95 % Confidence interval for β			
	β	Lower limit	Upper limit	p-value
(Constant)	00.711	−00.420	1.842	0.215
Intervention	00.158	00.002	00.314	0.048
Females	−00.028	−00.204	00.148	0.754
Age >40 years	00.041	−00.207	00.288	0.746
Receiving dolutegravir based regimen	−00.055	−00.435	00.324	0.773
High density lipoprotein cholesterol	00.005	−00.005	00.014	0.309
Baseline protein intake (calorie)	00.000	−00.001	00.000	0.181
Baseline adequate diversified dietary intake	00.033	−00.148	00.213	0.721
Baseline fat intake (calorie)	00.000	−00.001	00.000	0.426
Baseline fibre intake (gram)	00.001	−00.005	00.007	0.710
Waist circumference (centimeter)	−00.006	−00.017	00.005	0.266
Body mass index (kilogram/metre^2)	−00.001	−00.022	00.021	0.949

β, unstandardized coefficient.

In linear regression, the intervention was significantly correlated with changes in weight, BFP and percentage skeletal muscle mass after adjusting for baseline factors. Additionally, intervention was significantly correlated with ≥3 % weight reduction from baseline. Similar results have been reported in several studies, which demonstrating the substantial influence of interventions on body weight reduction [68,69]. This may have clinically significant implications for improving cardiometabolic risk markers [17,18,22]. Consequently, offering routine and successful lifestyle counselling could ensure that at-risk individuals receive timely and may help reduce obesity related health problems [70].

5. Limitations

This study had several limitations. This study focused solely on adults with overweight and obesity, which may have restricted the applicability of the findings to the general population. We did not assess cardiovascular disease indicators, such as lipid profiles, or metabolic indicators like fasting blood sugar at the completion follow up, which may limit our evaluation of metabolic and cardiovascular outcomes. Nearly one-fourth of participants in the intervention group reported economic constraints, which may have limited their access to a variety of healthy, diversified, and fiber-enriched foods essential for supporting weight loss and management. Additionally, the baseline data on food frequency, 24-h dietary recall, and physical exercise were self-reported, which could have introduced inaccuracies and response bias.

6. Conclusion

This study demonstrates that lifestyle counselling led to significant changes in weight and body composition over six months in adults with overweight or obesity receiving ART. Additionally, lifestyle modification interventions were notably associated with changes in weight, BFP, percentage skeletal muscle mass and a weight loss of ≥3 % from baseline. Therefore, the routine provision of lifestyle counselling for individuals with overweight or obesity on ART could help mitigate obesity-related health risks and enhance clinical outcomes. In addition, well-controlled trials with larger sample size and sex stratifications are essential to assess the long-term effects of lifestyle interventions on cardiometabolic risk factors in this population.

Clinical key take away messages

- Lifestylecounselling resulted in significant reductions in weight, FM, VF, and BFP.
- The counselled group showed an increase in FFM and skeletal muscle mass.
- Lifestyle counselling correlated with achieving ≥3 % weight loss.

Declaration of artificial intelligence (AI) and AI-assisted technologies

The authors did not use AI tools during the preparation of this work.

Author contributions

Agete Tadewos Hirigo, Zelalem Debebe, Daniel Yilma and Ayalew Astatkie conceptualized and designed the study. Agete Tadewos Hirigo and Moges Derbe contributed to data collection. Agete Tadewos Hirigo, Zelalem Debebe, Daniel Yilma and Ayalew Astatkie conducted data analysis and drafted the initial manuscript. Zelalem Debebe, Daniel Yilma and Ayalew Astatkie provided supervision, interpreted the data, critically revised the manuscript and gave final approval for publication.

All authors reviewed and approved the final manuscript

Ethics review

The study protocol was approved by the Institutional Review Board of the College of Natural and Computational Sciences at Addis Ababa University (Approval No: IRB/07/14/2022). All participants were provided with information regarding the research objectives and potential benefits, and written informed consent was obtained.

Trial registration

This clinical trial was retrospectively registered with the Thai Clinical Trials Registry on September 5, 2024 (TCTR20240905007) and can be accessed at https://www.thaiclinicaltrials.org/show/TCTR20240905007.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Annexes

Annex-I: English version of the written information sheet and consent form

My name is _____, and I work for Agete Tadewos as a data collector. He is a clinical Nutrition Ph.D. student at Addis Ababa University's Center for Food Science and Nutrition. With the financial support of Addis Ababa University, he is undertaking a study on Cardiometabolic risks among adults living with HIV on antiretroviral therapy in southern Ethiopia following test-and-treat implementation: Disease Burden, Determinants and Effects of Lifestyle Counseling. I would very much appreciate your participation in this study, as you were chosen at random to participate, and about 576 HIV-positive people on first-line ART will be invited to participate. The information you provide us is incredibly significant and very beneficial since it will serve as a baseline and it is critical to take early measures before patients develop non-HIV-associated chronic diseases.

Procedures: If you agree to participate in this study, I would want to ask you questions regarding socio-demographic, behavioral, clinical, psychiatric, and food desires. The interview will last about 15-20 minutes. In addition, I would like to measure your blood pressure, weight, height, waist, hip and neck circumferences. This data will allow us to assess the health status of HIV-positive people living in the study area, and the measures will be repeated to ensure consistency and accuracy. Furthermore, if you consent, a medical laboratory technologist will draw 4-5 milliliters of venous blood to determine lipid profiles, fasting glucose and hemoglobin A1c (HbA1c) level.

Risks: Participating in this study, in my opinion, poses no risk to you. There should be no discomfort at all for you. When the vein puncture is performed, you may feel some minor discomfort, but this is momentary and will fade away within a few minutes.

Benefits: Participating in this research project may not benefit you personally, but it may be essential to improve healthcare services for people receiving antiretroviral agents.

Compensation: You will not be paid for participating in this study. I appreciate your participation in this study.

Confidentiality: I want to assure you that the information you offer us is confidential and will only be used for this research. On the questionnaire, we will use a number instead of your name. Your name and other identifying information will not be shown when we present this study to others or publish its findings. The questionnaires will be kept in secured cabinets for up to four years, and the data will be saved on password-protected computers.

Voluntary Participation and Withdraw: Participation in this study is voluntary, and you may opt-out at any time throughout the interview. You have the option of refusing to speak with us or asking us to leave, and if you do choose to participate, you can stop the interview at any point or skip any questions that you do not wish to answer. Whether or not you choose to participate does not affect the services you may receive from the health system.

Contact Persons: In based upon the information, I believe you are aware that your involvement in the research's success is critical, and I appreciate your contribution to the study. I will be happy to answer any queries you may have. If you need additional information, call the research's principal investigator (Agete Tadewos) at 0913175126. Do you have any other questions? Would you be willing to participate in the study, please?

A. Yes B. No

I understand the benefits of the research and the responsibilities I will play in it. I have consented to participate in the research.

Signature (participant)_____Date_____

Name of data collector_____signature_____date_____

Annex-II: English version questionnaires

Name of interviewer _____ Date_____

ID No_____		**Card. No_____**	
Socio-demographic variables			
Q: No	**Questions**	**Response & code**	**Skip to Q…**
101	How old are you?	_____years	
102	What is the sex of the respondent?	Male Female	
103	What is your ethnic background?	Amhara Sidama Oromo Tigrie Wolayita Others(specific)_____	
104	What is your marital status?	Single Married Divorced Widowed/widower	
105	What is your residence?	Urban Rural	
106	What is the highest level of education you have completed?	No formal education Read and write Primary education (1-8) Secondary (9-10) College and above	
107	What is your occupation?	Employed (GOV/NGO) Self-employed Farmer Trader Daily laborer Pension Housewife Student Other (specify)_____	
108	What is your religion?	Orthodox Protestant Muslim Catholic Others specify_____	
109	Can you tell me the monthly income of the household?	_____in ETH birr	
Behavioral variables			
201	Have you ever consumed any alcohol such beer, Tella, Bordie, Tej, Arake, wine, korofe, borde spirits, beherawi, ye bale zaf?	No Yes	If no skip to Q 212
202	If yes for Q 201, have you consumed any alcohol within the past 12 months?	No Yes	
203	If yes for Q 201, have you stopped drinking due to health problems?	No Yes	

204	If yes for Q 201, how long ago did you stop drinking?	_____years or _____months	
205	If yes for Q 201, during in the past 12 months, how frequently have you had at least one standard alcoholic drink? a standard drink equivalent to 1 bottle beer /1 glass wine /1 shot ('malekia') Areki/1'birille'Tej/1 "tassa" Tella/ Korofe	Daily 5-6 days per week 3-4 days per week 1-2 days per week 1-3 days per month Less than once a month Never	
206	If yes for Q 201, have you consumed any alcohol within the past 30 days?		
207	If yes for Q 201, during the past 30 days, on how many occasions did you have at least one standard alcoholic drink? (Use Showcard)	_____occasions	
208	If yes for Q 201, during the past 30 days, when you drank alcohol, how many standard drinks on average did you have during one drinking occasion?	Number of times_____ Don't know_____	
209	If yes for Q 201, during each of the past 7 days, how many standard drinks did you have each day? (Use Showcard)	Number of times_____ Don't know_____	
210	If yes for Q 201, during the past 30 days, how many times did you have six or more standard drinks on a single drinking occasion? (Six for males and 4 for females)	Number of times_____ Don't know_____	
211	If yes for Q 201, do you remember how long ago it was, you have been started drinking alcohol?	Weeks _____ Months_____ Years _____	
212	Have you ever smoked tobacco products?	No Yes	If no skip to Q 218
213	If yes for Q 212, do you currently smoke any tobacco products, such as cigarettes, cigars, Gaya or pipes?	No Yes	
214	If yes for Q 212, do you currently smoke tobacco products daily?	No Yes	
215	If yes for Q 212, do you currently use any smokeless tobacco products such as (snuff, chewing tobacco or betel)?	No Yes	
216	If yes for Q 212, when did you completely quit smoking tobacco products?	_____years_____months _____weeks Don't know_____	
217	If yes for Q 212, do you remember how long ago it was, you have been started using tobacco products?	_____years	
218	Have you ever chewed Khat?	No Yes	If no skip to Q 301
219	If yes for Q 218, are you currently chewing Khat?	No Yes	
220	If yes for Q 218, during the last 30 days, on average how many days did you chew Khat?	Daily Weekly Less than a month	

		Others specify_____	
221	If yes for Q 218, how many Zurbas/"esire" do you chew on one of those days?	_____Zurba/essire	
222	If yes for Q 218, how long ago did you stop chewing Khat?	_____years_____months	
223	If yes for Q 218, do you remember how long ago it was, you have been started chewing Khat?	Weeks _____ Months_____ Years _____	
Physical activity variables			
301	During the **last 7 days**, did you do **vigorous** physical activities like heavy lifting, digging, aerobics or fast bicycling?	No Yes	If no skip to Q 303
302	If yes for Q 301, in a typical week, on how many days do you do vigorous-intensity activities as part of your work?	_____days	
303	If yes for Q 301, how much time do you spend doing vigorous-intensity activities at work on a typical day?	_____min/day	
304	Does your work involve moderate-intensity activity that causes small increases in breathing or heart rate such as brisk walking [or carrying light loads] for at least 10 minutes continuously?	No Yes	
305	If yes for Q 304, in a typical week, how many days do you do moderate-intensity activities as part of your work?	_____day	
306	If yes for Q 304, how much time do you spend doing moderate-intensity activities at work on a typical day?	_____hours_____ minutes	
307	**<u>Travel to and from places</u>** Do you walk or use a bicycle for at least 10 minutes continuously to get to and from places?	No Yes	
308	If yes for Q 307, in a typical week, on how many days do you walk or bicycle for at least 10 minutes continuously to get to and from places?	_____days	
309	If yes for Q 307, how much time do you spend walking or bicycling for travel on a typical day?	_____hours _____minutes	
310	**<u>Recreational activities</u>** Do you do any vigorous-intensity sports, fitness or recreational (leisure) activities that cause large increases in breathing or heart rate like [running or football, aerobics, fast bicycling, fast swimming] for at least 10 minutes continuously?	No Yes	
311	If yes for Q 310, in a typical week, on how many days do you do vigorous-intensity sports, fitness or recreational (leisure) activities?	_____days	

312	If yes for Q 310, how much time do you spend doing vigorous-intensity sports, fitness or recreational activities on a typical day?	_____hours _____ minutes	
313	If yes for Q 310, do you do any moderate-intensity sports, fitness or recreational (leisure) activities that cause a small increase in breathing or heart rate such as brisk walking, [cycling, swimming, and volleyball] for at least 10 minutes continuously?	No Yes	
314	If yes for Q 310, in a typical week, on how many days do you do moderate-intensity sports, fitness or recreational (leisure) activities?	_____days	
315	If yes for Q 310, how much time do you spend doing moderate-intensity sports, fitness or recreational (leisure) activities in a typical day?	_____hours_____ minutes	
316	**Sedentary behavior/ sitting time** How much time do you usually spend sitting or reclining on a typical day?	_____hours _____ minutes	
Diet-related variables *and Counseling on lifestyle and dietary management*			
401	Have you ever received counseling about lifestyle modification and dietary management from ART nurses?	No Yes	If no skip to Q 403
402	If yes for Q 401, how many times?	Single time Two times Repeatedly I don't remember	
403	How many days in a typical week do you eat fruit?	_____ days	
404	How many servings of fruit do you eat on one of those days? (serving, in this case, refers to slice or one full fruit e.g. orange, banana, mango, …)	0 1 2 3 4 ≥5	
405	How many days in a typical week do you eat vegetables?	_____days	
406	How many servings of vegetables do you eat on one of those days? (serving, in this case, refers to cups or "Chilfa") of vegetable stews)	0 1 2 3 4 ≥5	
407	Is it the correct amount that you consumed (servings of fruits and vegetables) on a typical day?	No Yes	
408	If "No" why not use the appropriate amount of FAV?	Due to economic issue Lack of access to get shortly Lack of desire to use them Others specify_____	
409	Are you aware of the daily recommended number of servings of fruits and vegetables?	No Yes	

410	If yes for Q 409, how many?	_____vegetables_____ fruit servings	
411	What type of oil or fat is most often used for meal preparation in your household?	Liquid vegetable oils Solid vegetable oils (Viking, Chief...) Sesame/Nug oil/Sunflower Sheno Lega, Shadi Lega Natural butter Other mention_____ I don't know	
412	How often do you add salt or a salty sauce, such as soya sauce to your food right before you eat it or as you are eating it	Always Often Sometimes Rarely Never Don't know	
413	How often is salt, salty seasoning or a salty sauce added in cooking or preparing foods in your household?	Always Often Sometimes Rarely Never Don't know	
414	How often do you eat processed food high in salt? By processed food high in salt, I mean foods that have been altered from their natural states, such as packaged salty snacks, canned salty food including pickles and preserves, salty food prepared at a fast-food restaurant, cheese, bacon, Mitmitta, and processed meat like Quanta	Always Often Sometimes Rarely Never Don't know	
415	How much salt or salty sauce do you think you consume?	Far too much Too much Just the right amount Too little Far too little Don't know	
416	What is your consumption status of flesh and dairy products?	Daily 4-6 days per week 2-3 per week 2-3 per month ≤ 1 day per month	
417	Have you ever observed any change in your food desire, food frequency or feeling of hungry after initiation/ switching to the current ART regimens?	No Yes	If no skip to Q 501
418	If yes for Q 419, what about your food desire?	highly decreased Decreased Slightly increased Moderately increased Highly increased	
419	If yes for Q 419, have you ever observed any change in your food intake frequency after the initiation/ switching to these ART regimens?	No Yes	

420	If yes for Q 419, how many meals do you eat per day?	One meal a day Two meals a day Three meals a day Four meals a day More than four meals a day	
421	If yes for Q 419, have you ever observed any change in your food intake amount after the initiation/ switching to the current ART regimens?	highly decreased Decreased Moderately increased Highly increased	
422	If yes for Q 419, do you feel hungry frequently?	No Rarely Some times Most of the time All of the time	
Psychiatric related variables (Anxiety and Depression questions)			
501	I feel tense or 'wound up'	Most of the time A lot of the time From time to time, occasionally Not at all	**Anxiety**
502	I get a sort of frightened feeling like butterflies in the stomach:	Not at all Occasionally Quite often Very often	
503	I get a sort of frightened feeling as if something awful is about to happen:	Very definitely and quite badly Yes, but not too badly A little, but it doesn't worry me Not at all	
504	I feel restless as I have to be on the move:	Very much indeed Quite a lot Not very much Not at all	
505	Worrying thoughts go through my mind:	A great deal of the time A lot of the time From time to time, but not too often Only occasionally	
506	I get sudden feelings of panic:	Very often indeed Quite often Not very often Not at all	
507	I can sit at ease and feel relaxed:	Definite Usually Not often Not at all	
508	I still enjoy the things I used to enjoy:	Definitely as much Not quite so much Only a little Hardly at all	**Depression**
509	I have lost interest in my appearance:	Definitely I don't take as much care as I should I may not take quite as much care I take just as much care as ever	
510	I can laugh and see the funny side of things:	As much as I always could Not quite so much now Definitely not so much now	

		Not at all	
511	I look forward with enjoyment to things:	As much as I ever did Rather less than I used to Definitely less than I used to Hardly at all	
512	I feel cheerful:	Not at all Not often Sometimes Most of the time	
513	I can enjoy a good book or radio or TV program	Often Sometimes Not often Very seldom	
514	I feel as if I am slowed down	Nearly all time Very often Sometime Not at all	
515	Do you have sleep disorder (insomnia) after the initiation of ART drugs?	1. Nearly all time 2. Very often 3. Sometime 4. Not at all	
516	Do you have slowed thinking problem?	1. Nearly all time 2. Very often 3. Sometime 4. Not at all	
Clinical related variables			
601	Duration since HIV diagnosis?	_____years	
602	Duration since ART initiation?	_____months	
603	A participant's the most recent first-line ART regimen? *can be confirmed from the patient chart	TDF/DTG based TDF/EFV based AZT/EFV based	
604	Do you have a history of ART treatment changes?	No Yes	If no skip to Q 610
605	If yes for Q 604, how many times changed? *can be confirmed from the participants chart	One time Two times Three times	
606	If yes for Q 604, the previous regimen? *specify if more than one switch *can be confirmed from participants chart	TDF/EFV AZT/EFV TDF/NVP AZT?NVP other_____	
607	If yes for Q 604, duration of ART treatment before switching? *can be confirmed from participants chart	_____year _____month	
608	If yes for Q 604, duration of ART treatment after switching? *can be confirmed from participants chart	_____year _____month	

609	If yes for Q 604, what was the reason for the regimen change?	Toxicity Virological failure WHO recommendation	
610	Have you ever had your blood pressure measured by a doctor or other health worker?	No Yes	
611	Have you ever been told by a doctor or other health worker that you have raised blood pressure or hypertension?	No Yes	
612	Have you been told in the past 12 months?	No Yes	
613	In the past two weeks, have you taken any drugs (medication) for raised blood pressure prescribed by a doctor or other health worker?	No Yes	
614	Has any of your family members (biological parents, siblings or children) ever had raised blood pressure or hypertension?	No Yes	
615	Have you ever had your blood sugar measured by a doctor or other health worker?	No Yes	
616	Have you ever been told by a doctor or other health worker that you have raised blood sugar or diabetes?	No Yes	
617	Have you been told in the past 12 months?	No Yes	
618	In the past two weeks, have you taken any drugs (medication) for diabetes prescribed by a doctor or other health worker?	No Yes	
619	Has any of your family members (biological parents, siblings or children) ever had raised blood sugar or Diabetes?	No Yes	
620	Have you ever had your cholesterol (fat levels in your blood) measured by a doctor or other health worker?	No Yes	
621	Have you ever been told by a doctor or other health worker that you have raised cholesterol?	No Yes	
622	Have you been told in the past 12 months?	No Yes	
623	In the past two weeks, have you taken any oral treatment (medication) for raised total cholesterol prescribed by a doctor or other health worker?	No Yes	
624	Has any of your family members (biological parents, siblings or children) ever had raised Cholesterol?	No Yes	
625	Have you ever had a heart attack or chest pain from heart disease (angina) or a stroke (cerebrovascular accident or incident)?	No Yes	

626	Are you currently taking aspirin regularly to prevent or treat heart disease?	No Yes	
627	Are you currently taking statins (Lovastatin/Simvastatin/Atorvastatin or any other statin) regularly to prevent or treat heart disease?	No Yes	
628	Have you ever been diagnosed with TB?	No Yes	If no skip to Q 631
629	If say "yes" which TB?	Pulmonary Extra-pulmonary	
630	If say "yes" when?	Before ART After ART	
631	Have you ever been treated with INH prophylactic treatment?	No Yes	
632	Have you taken cotrimoxazole prophylactic treatment?	No Yes	
633	The functional status of the participant at ART initiation	Working Ambulatory Bedridden	
634	The WHO clinical stage of the participant at ART initiation? *Can be confirmed from a chart	I II III IV	
635	Other comorbidities or OIs *Can be confirmed from a chart	Mention_____	
636	Participant's ART adherence rate? *Can be confirmed from a chart	Good Fair poor	

7. Patterns of dietary intake and diversity

7.1. A **one-week food frequency Questionnaire: Write the day of week _____ ID. No._____date_____**							
Food group	**More than one times /day**	**Once /day**	**5–6 times /week**	**3–4 times /week**	**2 times times /week**	**Once /week**	**Never**
Any **cereal** crops? bread, wheat, Teff, or any other foods made from millet, sorghum, maize, rice							
Aroot and tuber crops? Potatoes, sweet potato, yams, beat root, cassava or Enset and its products (kocho, Bulla….)							
Any **vegetables**? Spinach, carrot, cabbage, Pumpkin, kale, broccoli...							
Any **fruits**? Orange, apple, papaya, mango, pineapple, avocado, banana, lemon, strawberry.							
Pulses and legumes or nuts: beans, peas, lentils, chickpea, grass pea,							
Nuts and seeds: peanut, sesame, sunflower, flaxseeds							
Meat, poultry, offal: Sheep and goat, chicken, or other organ meats?							
Any Any **eggs**?							
Fish and sea foods?							
Milk and milk products, cheese, yogurt, milk or other milk products							
Oil, fat or butter?							
Sugar, honey or sweets/soft drinks?							
Any other foods, such as condiments, coffee, tea?							

7.2. 24-hour Dietary Intake Questionnaire

I would like to ask you about some liquids, solid or semi-solid food that you may have had yesterday during the day or at night. All food that you ate including drinks, snacks, sauces, spices, and others will need to be recalled and listed. There is no right or wrong answer in this interview; you only need to tell me what you actually ate. Do you have any questions? If not, let's start.

Form for Recording the Interactive 24-hour Recall

Code_____Interviewer name _____ sex_____ age_____ day of food eaten_____ day of interview _____						
Time	Place eaten: home/out	Food or drink	Description and cooking method	Amount eaten	Weight Equivalent (g)	Food code
Breakfast						
Snacks						
Lunch						
Snacks						
Dinner						
Snacks						

7.3. Description of food and ingredients (Recipe form)

Food or drink	**Description and cooking method**	**Amount prepared (by equipment)**	**Amount you ate (by equipment)**	**Equivalent weight (in gram)**
	Ingredient and cooking method			
	Ingredient and cooking method			
	Ingredient and cooking method			
	Ingredient and cooking method			
	Ingredient and cooking method			
	Ingredient and cooking method		-	

701.	Have you heard/ receive information about the importance of diversified diet?	☐Yes	☐No
702.	If Yes from where? mention		
703.	Have you got sufficient counseling on diversified diet utilization?	☐Yes	☐No
704.	Do you have any challenge to use diversified diet?	☐Yes	☐No
705.	If yes, what type of challenge do you have?	☐ Economical ☐Knowledge and skill gap ☐ cultural ☐ others mention_____	
706.	Family size		
707.	Probe for alcohol:	☐Yes	☐No
708.	Probe for sickness	☐Yes	☐No
709.	Did sickness affect appetite?	☐Yes	☐No
710.	If yes, how?	☐Increase	☐decrease
711.	Was food intake unusual?	☐Yes	☐No
712.	If yes, how was it unusual?	☐Increase	☐decrease
713.	Was it a feast day?	☐Yes	☐No
714.	Was it a market day?	☐Yes	☐No
715.	Was it weakened?	☐Yes	☐No
716.	Was it a fasting day?	☐Yes	☐No
717.	Have you skipped meals?	☐Yes	☐No
718.	If yes which one?	☐Break fast ☐Lunch	☐Snacks ☐Dinner
719.	Probe tablets	☐Yes	☐No
720.	If yes	Mention_____	

English version of anthropometric, cardiovascular and laboratory-related measurements

Name of interviewer _____Date_____

ID No_____	**Card. No_____**		
Anthropometric, blood pressure	First measure	Second measure	Remarks
801 Current body weight [in Kg]?	_____	_____	
802 BMI (in kg/m^2)	_____	_____	
803 Height [in meter]?	_____	_____	
804 Sitting height [in meter]?			
805 Waist circumference (in cm)?	_____	_____	
806 Hip circumference (in cm)?	_____	_____	
807 Neck circumference (in cm)?	_____	_____	
808 Current Systolic/diastolic BP (mmHg)?	_____&_____	____&_____	
809 Current Heart rate (bit/minute)?	_____	_____	
Bioimpedance Result			
901 Body fat (in %)?	_____	_____	
902 Skeletal muscle%	_____	_____	
903 Visceral fat level?	_____	_____	
904 Biological age (in years)?	_____	_____	
Laboratory measurement			
101 Fasting blood glucose(in mg/dL)	_____		
102 Glycated hemoglobin (%)	_____		
103 Total cholesterol (in mg/dL)	_____		
104 Triglyceride (in mg/dL)	_____		
105 HDL-cholesterol (in mg/dL)	_____		
106 LDL-cholesterol (in mg/dL)	_____		

Annex-IV: English Version data collection checklist

										S.no
										Card.no
										Sex[M for male; F for female)
										Age (in years)
										Duration since HIV diagnosis (in years)
										Duration since ART initiation (in yrs.)
										Marital status (1: single, 2:married, 3:divorced 4: Widow/er
										Residence (1: rural, 2: Urban)
										Educational status(1: unable to R&W, 2: informal, 3: primary, 4: 2dry , 5≥college)
										Occupation (1:employed, 2:farmer, 3:housewife, 4:unemployed, 5daily laborer,
										Religion (1: orthodox, 2:protest, 3:muslim, 4:cathol, 5:others)
										History of smoking (1:No, 2: Yes)
										History of alcoholism (1:No, 2: Yes)
										CD4cells count at baseline? (cells/mm^3)
										Viral load at 6 months?(copies/ml)
										CD4cells at initiation/ switching to recent ART regimen? (cells/mm^3)
										The viral load during initiation/ switching to a recent ART regimen? (cells/mm^3)
										History of chronic disease ((1:No, 2: Yes)
										History of TB Infection(1:No, 2: Yes)
										Use of Anti-TB drugs (1:No, 2: Yes)
										INH prophylactic treatment (1:No, 2: Yes)

																S.no
																Card.no
																Cotrimoxazole PPT? (1:No, 2: Yes)
																OIs other than TB (1:No, 2: Yes)
																ART adherence rate? (good, fair, bad)
																Baseline ART regimen 1EFV, 2NVP, 3 DTG
																ART changed? (1:No, 2: Yes)
																Reason for ART change (1:toxi, 2: failure, 3: other
																Number of switches (1, 2, 3)
																Current regimen (1:EFV, 2:DTG)
																Bodyweight at baseline of initiation/ switching (Kg)
																Bodyweight at 6 months (Kg)
																Bodyweight at 12 months(Kg)
																Bodyweight at 18 months (Kg)
																Bodyweight at 24 months (Kg)
																Current Bodyweight (Kg)
																WHO stage during start of current Regimen (I, II, III, IV)

Annex-V: በአማርኛ ቋንቋ የተዘጋጀ የጥናቱ መረጃ መስጫና የስምምነት መሙያ ቅጽ

ሰላም! ጤና ይስጥልኝ፤ ስሜ ---------- ይባለል፤ እኔ የዚህ ጥናት መረጀ ሰብሳቢ ሲሆን የጥናቱ ባለቤት በአድስ አበባ ዩኒቨረሲቲ የምግብ ሳይንስ እና ኒዉትሪሽን ት/ት ክፍል **የክሊኒካል ኒዉትሪሽን ፒ.ኤች. ዲ. ዲግሪ** ተማሪ በሆኑት አቶ አጌጠ ታድዎስ የሚካሄድ ነዉ። የጥናቱ ዓላማም በሲዳማ ክልል ሐዋሳ ከተማ አስተደደር ስር በሚገኙ ፀረ-ኤች አይ ቪ የህክምና አገልግሎት በሚሰጡ ሆስፒታሎችና ጤና ጠቢያዎች የፀረ-ኤች አይ ቪ መድሓኒት በሚጠቀሙ አዋቂዎች ላይ የሚከሰቱ የዉፍረት፡ የደም ግፍት፡ የስኪርና የሰዉነት ቅባት ዓይነቶች ስርዓተ-ዉህደት ችግሮችና መንስኤዎቸዉ እናም የስፖርታዊ እንቅስቃሴና የአመጋገብ ምክር አገልግሎት በሚያመጡዉ ለዉጥ ላይ ምርምር ለመድረግ ሲሆን ጥናቱ የሚደገፈዉ በአድስ አባበ ዩኒቨረሲቲ ነዉ። እርስዎ በብድብድግ ለጥናቱ ከተመረጡ 576 ተሳታፊዎች መካከል አንዱ ሲሆኑ በዚህ ጥናት ዉስጥ ስለታሳተፉ እናደንቃለን። በተጨማሪም የሚሰጡት መረጃ ወደፊት ለሚደረጉ ለሌሎች ተከታታይ ጥናቶች እንደ መነሻ መረጀ በመሆን ይጠቅማል::

የአሰራር ሀደት፡ በዚህ ጥናት ዉስጥ ለማሳተፍ ከተስማሙ ስምምነቱን መረዳትና ማስማማትዎን በፊርማ መግለጽ ይገባዎታል። ከዚያም በኋላ መረጀ ሰበሳቢዉ ለጥናቱ ግብአት የሚሆን መጠይቆችን ይጠይቅዎታል:: ስምዎትን መናገር አያስፈልግዎትም። የሚሰጡት መረጀ ምስጥራዊነቱ ይጠበቃል፤መጠይቁ በጠቅላላ ከ 15-20 ደቂቃ ያህል ጊዜዎትን ይሻማል፤ ሌላዉ የእርስዎን ደም ግፍት፤ ክብደት፤ ቁማት፡ ወገብና የዳሌ ዙርያ መጠን እንለካለን፤ ምናልባት አስፈለጊ ሲሆን ለዉጤቱ ጥራት ልኬቱን ልንደግም እንችላለን። በተጨማሪ ለስኳር ፡ ለ ኮሌስትሮልና፤ ለግላይኬትድ ሄሞግሎቢን ምርመራ የሚሆን ከ 3-4 ሲሲ ደም የላቦራቶሪ ባላሙያ ከእጅዎት ይወስደል።

ሊከሰቱ ሰለሚችሉ ሰጋቶች ወይም የምቾት መጉደሎች: በእኔ አመለካከት በዚህ ጥናት በማሳተፍዎ ምንም አሉታዊ ጎን የለም፡ ምናልባት ደም ሲወሰድ የተወሰነ ጊዜያዊ ያለመመቻቸት ስሜት ሊሰማዎት ይችላል፡ ነገር ግን ወድያዉ በጥቂት ደቂቃ ዉስጥ የሚጠፈ ስሜት ነዉ።

ጠቀሜታ: በዚህ ጥናት ላይ በመሳተፍዎ ቀጥተኛ የሆነ ጥቅም ላያገኙ ይችላሉ:: ነገር ግን መንስኤ ችግሮችን ማወቅ ፀረ-ኤች.አይ.ቪ /ኤድስ መድሓኒትና የህክምና ክትትል ለሚያደርጉት የጤና አገልግሎቱን ለማሻሸል በሚደረገዉ ስትራቴጂዎች ላይ ያግዛል::

የተሳትፎ ማበረታቻዎች/ክፊያ: ለተሳትፎዎ እጅግ እያመሰገንን በጥናቱ በመሳተፊዎ የሚሰጥ ምንም ዓይነት ማበረታቻ/ክፍያ የለም::

ሚስጥር ስለመጠበቅ፡ ላረጋግጥዎ የሚፈልገዉ ነገር ቢኖር ለዚህ ጥናት የሚሰበሰብ መረጀ በሚስጥር በሚገባ ይጠበቃል:: የሚሰበሰባዉ መጠይቅ የእርስዎ ለመሆኑ ስም ወይም መለያ አይኖረዉም:: መረጃዉ እስከ አረት ዓመት የሚቀመጥ ስሆን በዋናዉ ተመራማሪዉ ፋይል ተደርጎ በቁልፍ የሚቀመጥ ስሆን ኮምፒተሩም በፓስ-ወርድ ተቆልፎ የሚቀመጥ በመሆኑ ሌላ ሰዉ ሊያገኘዉ አይችልም::

በጥናቱ የመሳተፍ ወይም ራስን ከጥናቱ የማግለል መብት: በጥናቱ ላለመሳተፍ ከፈለጉ በዚህ ጥናት ያለመሳተፍ ሙሉ መብት አለዎት:: ከመጠየቁ ዉስጥ ጥቂት ጥያቄዎችን ወይም በሙሉ ያለመመለስ መብትዎ የተጠበቀ ነዉ፤ መጠይቁን ባለመመለስዎ ከዚህ የጤና ተቋም በሚያገኙት የጤና አገልግሎት አሰጠጥ ላይ ምንም ዓይነት ዕንቅፋት አይኖርም።

ለተጨማሪ መረጃ: እንደኔ እምነት በተሰጠዎት መረጃ መሰረት ስለጥናቱ የተረዱና የእረሶ ተሳትፎ ወሰኝ መሆኑን በቂ ግንዛቤ ያገኙ ይመስላል እናም ስለተሳትፎዎ እያደነቅሁ ማንኛዉም ጥያቄ ቢኖርዎት መጠየቅ ይችላሉ። ስለዚህ ጥናት ተጨማሪ መረጃ ከፈለጉ በማንኛዉም ጊዜ የጥናቱን ባለቤት አጌጠ ታድዎስን በዚህ ስልክ በማግኘት ማነጋገር ይችላሉ (0913175126):: ሌላ ጥያቄ አለዎት?

የዚህ ጥናት ዓላማዉንና ጥቅሙ ተረድቼ እናም የእኔ ተሳትፎ ሚና ገብቶኝ በጥናቱ ለመሳተፍ፤

ሀ. ፍቃደኛ ነኝ ለ. ፍቃደኛ አይደለሁም

የመጠይቁ ተሳታፊ ፊርማ ----------

የመረጃ ሰብሳቢ ሙሉ ስም----------ፊርማ ----------ቀን----------

Annex-VI: በአማርኛ ቋንቋ የተዘጋጀ የጥናቱ ቃለ-መጠይቅ

የመረጃ ሰብሳቢ ሙሉ ስም_____ቀን_____

መለያ ቁ።_____	**ካርድ፡ቁ_____**	
ማህበረዊ-ነክ መጠይቆች		
ተቁ	**ጥያቄዎች**	**ምላሽና ኮድ ቁጥር**	**ወደ ጥያቄ--ቁ--- ይለፉ**
101	አሁን ዕደሜዎ ስንት ነዉ?	_____ አመት	
102	የጥናቱ ተሳታፊ ፆታ?	ወንድ ሴት	
103	የየትኛው ብሄር አባል ነዎት?	አማራ ሲዳማ ኦሮሞ ትግሬ ወላይታ ሌላ(ይገለፅ)_____	
104	የትዳር ሁኔታዎ እንዴት ነው?	ያላገባ ያገባ የተፈታ/ች መበለት/ሚስቱ የሞተችበት	
105	የመኖሪያዎ ቦታ የት ነዉ?	ከተማ ገጠር	
106	የትምህርት ደረጃዎ?	ማንበብና ማፃፍ የማይችል ማንበብና ማፃፍ የሚችል 1ኛ ደረጃ(1-8) 2ኛ ደረጃ (9-12) ኮሌጅና ከዚያ በላይ	
107	እርስዎ የሚሰሩት/የሚተደደሩት ስራ ምንድነዉ ?	ተቀጣሪ (በመንግስት/በድርጅት የግል ሰረተኛ ግብርና ነጋዴ የቀን ሰራተኛ ጡረተኛ የቤትእመቤት ተማሪ ሌላ(ይገለፅ)_____	
108	ሃይማኖትዎ ምንድነው?	ኦርቶዶክስ ፕሮቴስታንት እስላም ካቶሊክ ሌላ(ይገለፅ)_____	
109	ወርሃዊ የቤተሰብ መተዳደሪያ ገቢዎ ምን ያህል ነዉ?	_____ብር ምንም ገቢ የለኝም ለመመለስ አልፈልግም	
በህሪይ ነክ መረጃዎች			

201	የአልኮል መጠጦችን ጠጥተዉ ያዉቃሉ? ለምሳሌ፡- ቢራ፣ ወይን፣ አረቄ፣ውስኪ፡ ቦርዴ፤ ኮሮፌ፤ ጠላ፤ጠጅ፤ብሄረዊ፤ወዘተ	አልጠጣም አዎን	“አልጠጣም” ወደ ጥያቄ፡ ቁ.212ይለፉ
202	ኣዎን ካሉ፤ በለፉት 12 ወራት የአልኮል መጠጦችን ወስደው/ጠጥተው ያውቃሉ?	አልጠጣሁም አዎን	
203	መጠጥ መጠጣትን በጤናዎ ምክንያት አቁመዋል?	የለም አዎን	
204	መጠጥን ካቆሙ ምን ያህል ጊዜ ሆነዎት?	_____ኣመት _____ወር _____ሳምንት	
205	በለፉት 12 ወራት በተደጋጋሚ በሚያስብል ስሌት ቢያንስ አንድ መደበኛ/ የአልኮል መጠን ያለው መጠጥን ለምን ያህል ጊዜ አዘውትረው ነበር? ለምሳሌ በትንሹ ቢራ 1-ጠርሙስ፡ ወይን 1-ብረጭቆ፡ አረቄ 1-ማላኪያ፡ ጠጅ 1-ቢሪሌ ወይም ጠላ/ኮሮፌ 1-ጣሳ፤	በየቀኑ በሳምንት ለ5 ወይም 6 ቀናት በሳምንት ከ3 እስከ 4 ቀናት በሳምንት 1 ወይም 2 ቀናት በወር ከ1 እስከ 3ቀናት በወር ከ 1 ቀን ያነሰ ቀናት በጭራሽ	
206	በለፉት 30 ቀናት የአልኮል መጠጥ ወስደው ወይም ጠጥተው ያውቃሉ?	የለም አዎን	
207	በለፉት 30 ቀናት በምን ያህል የተለያዩ ዝግጅቶች ላይ ቢያንስ አንድ መደበኛ የአልኮል መጠጥ ጠጥተዋል?	በቁጥር ይግለፁ_____ አላዉቅም_____	
208	በለፉት 30 ቀናት በአማካይ ለምን ያህል ጊዜ መደበኛ የአልኮል ይዘት ያላቸውን መጠጦች በግብዣ ኩነቶች ጠጥተዋል?	በቁጥር ይግለፁ_____ አላዉቅም_____	
209	በለፉት 30 ቀናት ብዛት ያለው መደበኛ የአልኮል መጠጥ በአንድ አጋጣሚ ጠጥተው ከሆነ የሁሉንም መጠጥ አይነት የጠጡትን ደምረው ቢነግሩኝ?	ትልቁ የጠጡት የመጠጥ መጠን _____ አላውቅም_____	
210	በለፉት 30 ቀናት ስድስት እና ከዚያ በላይ የሆኑ መደበኛ የአልኮል መጠጦችን በአንድ ግብዣ ብቻ ለምን ያህል ጊዜ ተጠቅመዋል? ለወንዶች፤ ስድስትና እና ከዚያ በላይ/ለሴቶችአራት እና ከዚያ በላይ	የተጠቀሙበት የጊዜ መጠን በቁጥር_____ አላውቅም_____	
211	ለምን ያህል ዘመን/ጊዜ መጠጥ ጠጥተዋል?	----------ሳምንታት ----------ወራት ----------አመታት	
212	በህይወት ዘመንዎ ሲጃራ አጭሰዉ ያውቃሉ? ለምሳሌ፡- ሲጃራ፣ ፒፖ፣ ጋያ	አላጨስኩም አዎን	“አላዉቅም” ወደ ጥያቄ፡ ቁ.218 ይለፉ
213	ባሁኑ ወቅት ሲጃራ ያጨሳሉ? ለምሳሌ፡- ሲጃራ፣ ፒፖ፣ ጋያ?	አላጨስም አጨሳለሁ	
214	ባሁኑ ወቅት ሲጃራ በየቀኑ ያጨሳሉ?	አላጨስም አዎን	

215	አሁኑ ወቅት ጭስ የሌላቸውን የትምባሆ ምርቶች በየቀኑ ይጠቀማሉ? ለምሳሌ፤ የሚሸተት፣ የሚታኝክ፣ በምግብ የሚወሰድ	የለም አዎን	
216	ማጨስ ካቆሙ ምን ያህል ጊዜ ሆነዎት?	_____ኣመት_____ወር _____ሳምንት አላዉቅም	
217	ለምን ያህል ዘመን/የትንባሆ ምርት ተጠቅማዋል?	_____ሳምንታት _____ወራት _____አመታት	
218	በህይወት ዘመንዎ ጫት ቅመው ያውቃሉ?	አላዉቅም አዎን	“አላዉቅም” ወደ ጥያቄ፡ ቁ.301 ይለፉ
219	በአሁኑ ወቅት ጫት ይቅማሉ?	አልቅምም አዎን	
220	በአማካይ በአንድ ወር ጊዜ ውስጥ ለምን ያህል ቀናት ጫት ይቅማሉ?	በየቀኑ/በየቀኑ በሚያስብል ሁኔታ በየሳምንቱ በየወሩ ሌላ ካለ ይጥቀሱ_____	
221	በሚቅሙበት ወቅት በአንድ ጊዜ ምን ያህል ዙርባ ወይም እስር ይቅማሉ?	_____ዙርባ/ እስር	
222	መቃም ካቆሙ ምን ያህል ጊዜ ይሆናል?	_____ኣመት _____ወር _____ሳምንት	
223	ለምን ያህል ዘመን/ጊዜ ጫት ቅመዋል?	_____ሳምንታት _____ወራት _____አመታት	
አካላዊ እንቅስቃሴን በተመለከተ የተብራራ ምላሽ የሚጠይቁ ጥያቄዎች			
301	የእርሰዎ ስራ ጠንካራ ጉልበት ብሎም ጥልቅ ትኩረት እና አንክሮ ይጠይቃል? ለማብራራት ያህል ስራዎ ብዙ ትንፋሽ የሚያስወጣና የልብን ምት የሚያስጨምሩ ማለትም(ከባድ ሸክሞችን ማንቀሳቀስ፣ መቆፈር ወይም የግንባታ ስራወችን ያጠቃልላል)? በተጨማሪም ቢያንስ ለ 10 ደቂቃዎች ያለማቋረጥ በስራ ላይ ሊቆዩ የሚችሉት ነዉ?	የለም አዎ	“የለም” ወደ ጥያቄ፡ቁ. 304 ይለፉ
302	ሁነኛ በተባለ አንድ ሳምንት ውስጥ ለምን ያህል ቀናት ጠንካራ ጉልበት፣ ጥልቅ ትኩረትና አንክሮ የሚጠይቅ ስራ ሰርተው ያውቃሉ?	_____ቀናት	
303	ሁነኛ በተባለ አንድ ቀን ውስጥ ለምን ያህል ሰአት ጠንካራ ጉልበት፣ ጥልቅ ትኩረትና አንክሮ የሚጠይቅ ስራ ይሰራሉ?	_____ ሰዓትና_____ደቂቃ	
304	የእርስዎ ስራ መለስተኛ ጉልበት ብሎም ብዙ ትንፋሽ የማያስወጣ መጠነኛ ትኩረትና አንክሮ	የለም አዎ	

	የሚፈልግ ስራ ነው? ለምሳሌ ፈጠን ያለ ርምጃ፣ ቀለል ያለ እቃ መሸከም (ቢያንስ ለ 10 ደቂቃ በተከታታይ)		
305	ሁነኛ በተባለ አንድ ሳምንት ውስጥ ለምን ያህል ቀናት መለስተኛ ጉልበት ብሎም ብዙ ትንፋሽ የማያስወጣ መጠነኛ ትኩረትና አንክሮ የሚፈልግ ስራ ሰርተው ያውቃሉ?	_____ ቀናት	
306	ሁነኛ በተባለ አንድ ቀን ውስጥ ለምን ያህል ሰአት መለስተኛ ጉልበት ብሎም ብዙ ትንፋሽ የማያስወጣ መጠነኛ ትኩረትና አንክሮ የሚፈልግ ስራ ያከናውናሉ?	_____ ሰዓትና_____ደቂቃ	
307	**<u>ከቦታ ወደ ቦታ መንቀሳቀስን በተመለከተ</u>** ከአንድ ቦታ ደርሶ ለመመለስ ቢያንስ 10 ደቂቃዎች የሚወስድ ጉዞን በእግር ወይም ብስክሌት በመጠቀም ይጓዛሉ?	የለም አዎ	
308	በአንድ ሁነኛ በተባለ ሳምንት ውስጥ ለምን ያህል ቀናት በእግርዎ ወይም ብስክሌት በመጠቀም ቢያንስ ለ10 ደቂቃወች የሚዎስድ ጉዞን ተጉዘዋል?	_____ ቀናት	
309	በአንድ ሁነኛ በተባለ እለት ለምን ያህል ሰአት በእግርዎ ወይም ቢስክሌት በመጠቀም ተጉዘዋል?	____ ሰዓትና_____ደቂቃ	
310	**<u>የመዝናኛ እንቅስቃሴዎችን በተመለከተ</u>** ለራስዎ በሚሰጡት የመዝናኛ ጊዜ ጉልበት የሚጠይቁ እና ትንፋሽ የሚያበዙ ስፖርቶችን ወይም የአካል ብቃት እንቅስቃሴዎችን ቢያንስ ለተከታታይ አስር ደቂቃ ያደርጋሉ? (ለምሳሌ- እግር ኳስ ይጫወታሉ፣ ቴኒስ፣ ሩጫ፣ ፈጣን ዋና፣ ጂም፣በሙዚቃ የታገዘ የሰውነት ማጎልመሻ	የለም አዎ	
311	በአንድ ሁነኛ በተባለ ሳምንት ውስጥ ለምን ያህል ቀናት ብርቱ እና አድካሚ ሰፖርት፣ የአካል ብቃት እንቅስቃሴ እና የሚያዝናኑ እንቅስቃሴዎችን ያደርጋሉ?	_____ ቀናት	
312	በአንድ ሁነኛ በተባለ ቀናት ውስጥ ለምን ያህል ሰአት ብርቱ እና አድካሚ ሰፖርት፣ የአካል ብቃት እንቅስቃሴ እና የሚያዝናኑ እንቅስቃሴዎችን ያደርጋሉ?	_____ ሰዓትና_____ደቂቃ	
313	መለስተኛ ጉልበት ብሎም ብዙ ትንፋሽ የማያስወጣ መጠነኛ ትኩረትና አንክሮ የሚፈልግ እና ቢያንስ በቀጣይነት ለ10 ደቂቃ የሚሰራ፤ ለምሳሌ ፈጠን ያለ የእግር ጉዞ፣ ሳይክል፣ ዋና፣ የእጅ ኳስ ያካሂዳሉ?	የለም አዎ	
314	በአንድ ሁነኛ በተባለ ሳምንት ውስጥ ለምን ያህል ቀናት ብርቱ እና አድካሚ ያልሆኑ ለምሳሌ ሰፖርት፣ የአካል ብቃት እንቅስቃሴ እና የሚያዝናና እንቅስቃሴዎችን ያደርጋሉ?	_____ ቀናት	

315	በአንድ ሁነኛ በተባለ ቀን ውስጥ ለምን ያህል ሰአት ብርቱ እና አድካሚ ያልሆኑ ለምሳሌ ሰፖርት፣ የአካል ብቃት እንቅስቃሴ እና የሚያዝናኑ እንቅስቃሴዎችን ያደርጋሉ?	_____ ሰዓትና_____ደቂቃ	
316	**<u>ብዙ እንቅስቃሴ ያለማድረግ ባህሪያት</u>** ሁነኛ በሚባል ቀን ለምን ያህል ሰአት ቁጭ ወይም ጋደም ይላሉ?	_____ ሰዓትና_____ደቂቃ	
የአመጋገብና ሰዉነት እንቅስቃሴ የምክር አገልግሎትና አመጋገብን በተመለከተ			
401	አመጋገብንና የሰዉነት እንቅስቃሴን በተመለከተ የምክር አገልግሎት ከ ኤአርቲ ነርሶች ያገኛሉ?	የለም አዎ	“የለም” ወደ ጥያቄ፡ቁ. 403 ይለፉ
402	አዎን ካሉ ስንት ጊዜ የምክር አገልግሎት አግኝታዋል?	አንዴ ብቻ ሁለት ጊዜ በተደጋጋሚ አላስታዉስም	
403	በአንድ ሁነኛ ሳምንት ለምን ያህል ቀናት ፍራፍሬ ተመግበዋል?	_____ ቀናት	
404	ፍራፍሬ በተመገቡበት ባንዱ ቀን ውስጥ ምን ያህል የገበታ አቅርቦትዎ ፍራፍሬዎችን ያካተተ ነበር? (ለምሳሌ፡- የተከፈለ ወይም አንድ ሙሉ ማንጎ፣ ብርቱካን፣ ፓፓዬ የመሳሰሉትን ማለቴ ነው)	0 1 2 3 4 ≥5	
405	በአንድ ሁነኛ ሳምንት ለምን ያህል ቀናት አትክልቶችን ተመግበዋል?	_____ ቀናት	
406	አትክልቶችን በተመገቡበት ባንዱ ቀን ውስጥ ምን ያህል የገበታ አቅርቦትዎ አትክልቶችን ያካተተ ነበር? (ለምሳሌ፡-በጭልፋ፣ በማንኪያ....)	0 1 2 3 4 ≥5	
407	በቀን የሚመገቡት የአትክልትና የፍረፍሬ ገበታ አቅርቦትዎ በቂ ነዉ ብለዉ ያምናሉ?	የለም አዎን	
408	የሚመገቡት የአትክልትና ፍረፍሬ ገበታ አቅርቦትዎ በቂ አይዶለም ካሉ ምክንያቱ ምንድነዉ?	ከገንዘብ እጥረት የአትክልትና ፍረፍሬ በቅርበት ካለማግኘት የአትክልትና ፍረፍሬ ፍላጎት ከማጣት ሌላ ይጠቀስ_____	
409	በቀን የሚመገቡት የአትክልትና የፍረፍሬ ገበታ መጠን ያዉቃሉ?	የለም አዎን	
410	አዎን ካሉ ምን ያህል ነዉ?	_____የአትክልትና _____የፍረፍሬ ገበታ	
411	በአብዛኛው ጊዜ በቤተዎ ውስጥ ምግብ ሲዘጋጅ የሚጠቀሙት ዘይት ወይም ቅባት ምን አይነት እንደሆነ ይምረጡ?	የአትክልት ዘይት ጠጣር (የሚረጋ) የአትክልት ዘይት (ቫይኪንግ፣ ቺፍ) የሰሊጥ/የኦግ/የሱፍ ዘይት ቅቤ ሸኖ ለጋ/ ሻዲ ለጋ ሌላ ካለ ይጥቀሱ_____ አላውቅም	

412	በምግብዎ ውስጥ ጨው፣ የሶያ ጨው፣ የቲማቲም ሶስ ምን ያህል አዘውትረው ይጠቀማሉ ከምግብ በፊት ወይም እየተመገቡ እያለ?(አንድ መልስ ብቻ ይምረጡ)	ሁልጊዜ ብዙውን ጊዜ አንዳንድ ጊዜ አልፎ አልፎ በጭራሽ አላውቅም	
413	በቤትዎ ውስጥ ምግብ በሚሰሩበትና በሚያዘጋጁበት ወቅት ጨዋማ የሆነ፣ የጨው ማጣፈጫ፣ የቲማቲም ሶስ የሆነ ወይም የሾርባ ጨው ምን ያህል ጊዜ ይጨምራሉ?	ሁልጊዜ ብዙውን ጊዜ አንዳንድ ጊዜ አልፎ አልፎ በጭራሽ አላውቅም	
414	ከፍተኛ የጨው መጠን ተጨምሮባቸው የተዘገጁ ምግቦችን ምን ያህል ያዘወትራሉ? ይህን ስል ምግብን ለማቆየት ሲባል ክፍተኛ የጨው መጠን በምግብ ውስጥ ይጨመራል ለምሳሌ፡- የታሸጉ ምግቦች፣ ቱና፣ የድንች ጥብስ፣ ቋንጣ፣ ቺዝ የመሳሰሉትን ለማለት ፈልጌ ነው።	ሁልጊዜ ብዙውን ጊዜ አንዳንድ ጊዜ አልፎ አልፎ በጭራሽ አላውቅም	
415	የሚጠቀሙት የጨው እና የሶያ ጨው መጠን ምን የህል ነው ብለው ያስባሉ?	እጅግ በጣም ብዙ በጣም ብዙ ትክክለኛውን መጠን አነስተኛ መጠን እጠቀማለሁ አልጠቀምም ማለት ይቻላል አላውቀውም--	
416	የስጋና የእንስሰት ተዋፅኦ አመጋገብዎት ምን ይመስለል?	በየቀኑ ከ 4-6 ቀነት በሰምንት ከ 2-3 ቀነትበሰምንት ከ 2-3 ቀነትበወር ≤ 1 ቀን በወር	
417	አሁን የሚወስዱትን የፀረ-ኤች አይ ቪ መድኃኒት መጠቀም ከጀመሩ ወድህ የምግብ ፍላጎትዎ ላይ ለዉጥ አለ?	የለም አዎን አለ	“የለም” ወደ ጥያቄ፡ቁ. 501 ይለፉ
418	አዎን ካሉ የምግብ ፍላጎትዎ ምን ይመስለል?	ቀንሶአል ትንሽ ጨምሮአል በመጠኑ ጨምሮአል በጠም ጨምሮአል	
419	አሁን የሚወስዱትን የፀረ-ኤች አይ ቪ መድኃኒት መጠቀም ከጀመሩ ወድህ በቀን የምግብ ድግግሞሽ ለዉጥ አለ?	የለም አዎን አለ	
420	አዎን ካሉ የሚመገቡት ስንት ጊዜ ይሆናል?	በቀን አንድ ጊዜ በቀን ሁለት ጊዜ በቀን ሶስት ጊዜ በቀን አረት ጊዜ በቀን ከአረት ጊዜ በላይ	

421	አሁን የሚወስዱትን የፀረ-ኤች አይ ቪ መድኃኒት መጠቀም ከጀመሩ ወድህ የሚመገቡት ምግብ መጠን ምን ይመስላል?	በጠም ቀንሶአል ቀንሶአል በመጠኑ ጨምሮአል በጠም ጨምሮአል	
422	የራሃብ ስሜት ቶሎ ቶሎ ይሰማዎታል?	የለም አልፎ አልፎ ይሪባኛል አንደንዴ ይሪባኛል ብዙ ጊዜ ይሪባኛል ሁሌ ይሪባኛል	
የአዕምሮ ጤንነት ሁኔታ መጠይቆች (የጭንቀትና የድብርት(ቁዛማ) ጥያቄዎች)			
501	የመጨነቅ/የመወጠር ስሜት ምን ያህል ይሰማዎታል?	በጠም ብዙ ጊዜ ብዙ ጊዜ አልፎ አልፎ ምንም አይሰማኝም	
502	ሆድ አካበቢ የሚሰማ የመደንገጥ/የመሸበር ስሜት ይሰማዎታል?	ምንም አይሰማኝም አልፎ አልፎ ብዙ ጊዜ በጠም ብዙ ጊዜ	
503	አንድ መጥፎ ነገር ሊያገጥምዎ የተቃረበ የሚመስል የፍረሀት ስሜት ይሰማዎታል?	እጅግ በጠም ይሰማኛል በጠም ይሰማኛል በጥቂቱ ይሰማኛል ምንም አይሰማኝም	
504	አንድ ቦታ መሄድ ያለብዎ ይመስል ተረጋግቶ መቀመጥ ይቸግርዎታል?	በጠም ብዙ ጊዜ ይቸግረኛል ብዙ ጊዜ ይቸግረኛል ብዙም አይቸግረኝም ምንም አይቸግረኝም	
505	ጭንቀትን የሚያጭሩ ሀሳቦች በአእምሮዎ ምን ይህል ጊዜ ይመላለሳሉ?	በጠም ብዙ ጊዜ ይቸግረኛል ብዙ ጊዜ ይቸግረኛል አብዛኛዉን ጊዜ ባይሆንም አልፎ አለፎ አንደንዴ ብቻ	
506	በድንገት የመደንገጥ/የመሸበር ስሜት ይሰማዎታል?	በጠም ብዙ ጊዜ ይሰማኛል ብዙ ጊዜ ይሰማኛል አልፎ አልፎ ይሰማኛል ምንም አይሰማኝም	
507	ተረጋግተዉ መቀመጥ እና ዘና ማለት ይችላሉ?	ሁሌም እችላለሁ አብዛኛዉን ጊዜ እችላለሁ ብዙዉን ጊዜ አልችልም ምንም አልችልም	
508	ቀደም ሲል ያስደስቱ የነበሩ ነገሮች አሁን ምን ያህል ያስደስታዎታል?	አሁንም እንደድሮዉ ያስደስቱኛል? ከድሮዉ ትንሽ ቀንሷል በጥቂቱ ያስደስቱኛል ጭራሽ አያስደስቱኝም	
509	ለአለባበስዎ ትኩረትን መስጠት አቁመዋል?	አዎን ምንም ትኩረት እየሰጠሁ አይዶለሁም የምፈለገዉን ያህል ትኩረት እየሰጠሁ አይዶለሁም	

		ድሮ ከሚሰጠዉ ትኩረት በጥቂቱ ያነሰ ትኩረትን እሰጣለሁ ሁሌም የምሰጠዉን ትኩረት እሰጠለሁ	
510	መሳቅና የነገሮችን አስቂኝ ጎን ማየት ይችላሉ	አብዛኛዉን ጊዜ እችላለሁ እንደድሮዉ ባይሆን እችላለሁ በጥቂቱ እችላለሁ ምንም አልችልም	
511	መጪ ነገሮችን በደስታ ይጠብቃሉ?	አዎ ሁሌም በተለመደዉ/በድሮ መጠን እጠብቃለሁ ከድሮዉ/ከተለመደዉ በጥቂቱ ባነሰ መጠን እጠብቃለሁ ከድሮዉ/ከተለመደዉ ባነሰ መጠን እጠብቃለሁ ምንም በደስታ አልፎብቅም	
512	ደስተኛ ነዎት?	ምንም ደስተኛ አይደለሁም ብዙ ጊዜ ደስተኛ አይደለሁም ብዙዉም ባይሆን ደስተኛ ነኝ አብዛኛዉን ጊዜ ደስተኛ ነ ኝ	
513	በሬድዮ፡ በቴሌቪዥን ወይም መፅሐፍ በማንበብ ራስዎን ያስደስታሉ?	አዎን ብዙ ጊዜ ብዙም ባይሆን አዎ አልፎ አልፎ በጠምአልፎ አልፎ	
514	ስራዎትን ሲያከናዉኑ ወዘተ ፍጥነትዎ ምን ያህል የቀነሰ ይመስልዎታል?	እጅግ በጠም ብዙ ጊዜ በጠም ብዙ ጊዜ አልፎ አልፎ ምንም አልቀነሰም	
515	የፀረ-ኤች አይ ቪ መድኃኒት ከጀመሩ ወድህ እንቅልፍ ማጠት ያስቸግርዎታል?	1. እጅግ በጠም ብዙ ጊዜ 2. በጠም ብዙ ጊዜ 3. አልፎ አልፎ 4. የለብኝም	
516	አሁን የሚወስዱት የፀረ-ኤች አይ ቪ መድኃኒት ከጀመሩ ወድህ ነገሮችን በቶሎ ማስተወስ ያስቸግርዎታል?	1. እጅግ በጠም ብዙ ጊዜ 2. በጠም ብዙ ጊዜ 3. አልፎ አልፎ 4. አያስቸግረኝም	
የህክምናና ተዛማጅ መጠይቆች			
601	ኤች አይ ቪ ከተመረመሩና ቨይረሱ በደምዎ መኖሩን ካወቁ ምን ያህል ጊዜ ነዉ?	_____ዓመት	
602	የፀረ-ኤች አይ ቪ መድኃኒት ከጀመሩ ምን ያህል ጊዜ ይሆናል?	_____ወረት	
603	የፀረ-ኤች አይ ቪ መድኃኒት አሁን የሚወስዱት? *(ከካርድ ላይ የሚረጋገጥ)	ቲድኤፍ/ዲቲጅን ያማከለ ቲድኤፍ/ኢፋቪረንዚን ያማከለ ኤዚቲ/ኢፋቪረንዚን ያማከለ	
604	የፀረ-ኤች አይ ቪ መድኃኒት ተቀይሮ ያዉቃል?	የለም አዎን	“የለም” ወደ ጥያቄ፡ቁ. 610 ይለፉ
605	አዎን ካሉ የፀረ-ኤች አይ ቪ መድኃኒት ስንት ጊዜ ተቀይሮአል? *(ከካርድ ላይ የሚረጋገጥ)	አንዴ ሁለት ጊዜ	

		ሶስት ጊዜ	
606	የፀረ-ኤች አይ ቪ መድኃኒት ከማቀያሩ በፊት የሚጠቀሙት መድሓኒት? *(ከካርድ ላይ የሚረጋገጥ)	ቲድኤፍ/ኢፋቪረንዚንያማከለ ኤዚቲ/ኢፋቪረንዚን ያማከለ ቲድኤፍ/ኔቬረፒንን ያማከለ ኤዚቲ/ኔቬረፒንን ያማከለ ሌላ_____	
607	የመጀመሪያዉን የፀረ-ኤች አይ ቪ መድኃኒት ለምን ያህል ጊዜ ተጠቀሙ? (ከካርድ ላይ የሚረጋገጥ)	_____ዓመት _____ወር	
608	የአሁኑን የፀረ-ኤች አይ ቪ መድኃኒት መዉሰድ ከጀመሩ ምን ያህል ጊዜ ይሆናል? * (ከካርድ ላይ የሚረጋገጥ)	_____ዓመት _____ወር	
609	የፀረ-ኤች አይ ቪ መድኃኒት የተቀየረበት ምክንያት? *(ከካርድ ላይ የሚረጋገጥ)	በመመራዝ ምክንያት ቨይረሱ ታላምዶ በ WHO ምክር	
610	የደም ግፊት መጠንዎን በጤና ሙያተኞች ተለክተው ያውቃሉ?	የለም አዎን	“የለም” ወደ ጥያቄ፡ቁ. 614 ይለፉ
611	የደም ግፊት መጠንዎን ከፍ እንዳለ በጤና ሙያተኞች ተነግሮዎት ያውቃል?	የለም አዎን	
612	ባለፉት 12 ወራት የደም ግፊት መጠንዎ ከፍ ብሏል ተብለው ያውቃሉ?	የለም አዎን	
613	በለፉት ሁለት ሳምንታት በሀኪም የታዘዘ የደም ግፊት መድሀኒት ወስደዋል?	የለም አዎን	
614	በቤተሰብዎ ውስጥ የደም ግፊት በሽታ ያለበት ሰው ነበር(አለ)? ቤተሰብ፡ አባት፡ እናት፡ ወንድምና እህት፡ ልጆች	የለም አዎን	“የለም” ወደ ጥያቄ፡ቁ. 619 ይለፉ
615	በደምዎ ውስጥ ያለው የስኪር መጠን ተለክቶ ያውቃል?	የለም አዎን	
616	በደምዎ ውስጥ ያለው የስኪር መጠን በጤና ሙያተኛ ተለክቶ ከፍተኛ ነው ወይም የስኪር በሽታ አለበዎት ተብለው ያውቃሉ?	የለም አዎን	
617	ባለፉት 12 ወራት በደምዎ ውስጥ ያለው የስኪር መጠን ከፍተኛ ነው ወይም የስኪር በሽታ አለበዎት ተብሎ ተነግሮዎታል?	የለም አዎን	
618	በለፉት ሁለት ሳምንታት በጤና ሙያተኞች የታዘዘ የስኪር ህመም መድሀኒት እየወሰዱ ቆይተዋል?	የለም አዎን	
619	በቤተሰብዎ ውስጥ የስኪር በሽታ ያለበት ሰው ነበር(አለ)? ቤተሰብ፡ አባት፡ እናት፡ ወንድምና እህት፡ ልጆች	የለም አዎን	
620	በደም ውስጥ ያለውን የኮሌስትሮል ቅባት መጠን በጤና ሙያተኛ ተለክተው ያውቃሉ?	የለም አዎን	“የለም” ወደ ጥያቄ፡ቁ. 624 ይለፉ

621	በጤና ሙያተኛ በደምዎ ውስጥ ያለው የኮሌስትሮል ቅባት መጠን ከፍተኛ ነው ተብለው ያውቃሉ?	የለም አዎን	
622	ባለፉት 12 ወራት በጤና ሙያተኛ በደምዎ ውስጥ ያለው የኮሌስትሮል ቅባት መጠን ከፍተኛ ነው ተብለዋል?	የለም አዎን	
623	ባለፉት ሁለት ሳምንታት በጤና ሙያተኛ በደምዎ ውስጥ ያለውን ከፍተኛ የኮሌስትሮል ቅባት መጠን የሚያስተካክል በአፍ የሚወሰድ መድሃኒት ወስደዋል?	የለም አዎን	
624	በቤተሰብዎ ውስጥ ከፍተኛ የኮሌስትሮል ቅባት መጠን ያለበት ሰው ነበር(አለ)? ቤተሰብ፡ አባት፡ እናት፡ ወንድምና እህት፡ ልጆች	የለም አዎን	
625	የልብ ህመምና ተዛማጅ የደረት ህመም ፡ ወይም ድንገተኛ ስትሮክ አለዎት?	የለም አዎን	
626	የልብ ህመምን ለመከላከል አስፒሪን እየወሰዱ ነዉ?	የለም አዎን	
627	የኮሌስቴሮል መጠን መቀነሻ መድሃኒትን የልብ ህመምን ለመካላከል እየወሰዱ ነዉ?	የለም አዎን	
628	በቲቢ በሽታ ተይዘዉ ያዉቃሉ?	አለዉቅም አዎን	“የለም” ወደ ጥያቄ፡ ቁ. 631 ይለፉ
629	አዎን ካሉ የትኛዉን ቲቢ ተይዛዋል?	የሰንባ ቲቢ ከሰንባ ዉጪ ቲቢ	
630	አዎን ካሉ መቼ ነዉ የተያዙት?	የ HIV ዕድሜ መራዛሚያ መድሃኒት ከመጀመሬ በፊት የ HIV ዕድሜ መራዛሚያ መድሃኒት ከጀመርኩ ቦኋላ	
631	የቲቢ በሽታ መካለከያ/የህክምና (INH) መድሃኒት ወስደዉ ያዉቃሉ?	አልወሰድኩም አዎን ወስጄ አዉቃለሁ	
632	የአድር ባይ ህመሞች መካለከያ መድሃኒት (ባክትሪየም) ወስደዉ ያዉቃሉ?	አለዉቅም አዎን አዉቃለሁ	
633	የጤናዎት ሁኔታ የፀረ-ኤች አይ ቪ መድኃኒት ሲጀሚሩ?	እየሰረሁና እየተንቀሰቀስኩ ነበር ተመላላሽ ህመምተኛ ነበርኩ የአልጋ ቁራኛ ነበርኩ	
634	የፀረ-ኤች አይ ቪ መድኃኒት ስጀምሩ የነበረዉ የ WHO ክሊኒካል ደረጀ? *(ከካርድ ላይ የሚረጋገጥ)	I II III IV	
635	ሌሎች ተጎደኝ (አድር ባይ) ህመሞች ካሉ	ይገለፅ_____	
636	የታከሚዉ የፀረ-ኤች አይ ቪ መድኃኒት አወሳሰድ? *(ከካርድ ላይ የሚረጋገጥ)	ጥሩ ነዉ በቂ/ተመጣጠኝ ነዉ ደካማ ነዉ	

የምግብ አመገጋብን የተመለከቱ ጥያቄዎች							
አሁን ከተዘረዘሩት የምግብ አይነቶች ባለፈው ሳምንት ውስጥ ስንት ጊዜ ተመግበው እንደነበር እንጠይቆታለሁ። (መረጃ ሰብሳቢበምላሻቸው መሰረት (√) ምልክት ያስቀምጡ)							
የምግብ አይነት ዝርዝር	**በሳምነት የተበላበት ቀን ወይም ጊዜ**						
	በቀን ከ1 ጊዜ በላይ	**በቀን 1 ጊዜ ብቻ**	**በሳምንት 5-6 ቀን**	**በሳምንት 3-4ቀን**	**በሳምንት 2 ቀን**	**በሳምንት 1 ቀን ብቻ**	**በፍጹም አልበላሁም**
ዳቦ፣ እንጀራ፣ወይም ከጥራጥሬ ወይም እንደ በቆሎ፣ማሽላ፣ ዘንጋዳ፣ዳጉሳ፣ ስንዴ፣ገብስ፣ጤፍ የተዘጋጀ ምግብ							
ከድንች፣ስኳርድንች፣ሽንኩርትእናሌሎችስራስሮችየተዘጋጀ ምግብ							
እንሰት (ቆጮ፣ቡላ) የተዘጋጀ ምግብ							
ከአትክልት፣ አረንጓዴ ቅጠላቅጠል፣ሰላጣ፣ጥቅል ጎመን፣ የሀበሻ ጎመን የተዘጋጀ ምግብ							
ማንኛውም ፍራፍሬ (ማንጎ፣አቮካዶ፣ፓፓያ፣ሙዝ)							
ማንኛውም ከበሬ ስጋ፣ከበግ ስጋ፣ከፍየል ስጋ፣ከዶሮ ስጋ የተዘጋጀ ምግብ							
ማንኛውም ከእንቁላል የተዘጋጀ ምግብ							
ማንኛውም ጥሬ ወይም የተጠበሰ ዓሳ							
ከባቄላ፣ ሽንብራ፣አተር፣ ቦሎቄ፣ጓያ የተዘጋጀ ምግብ							
ከቅባት እህሎች፡ ተልባ፡ ኑግ፤ አቾሎኒ፤ ሱፍ የተዘጋጀ ምግብ							
አይብ፣እርጎ፣ወተት							
ዘይት፣ቅቤ፣ስብ ያለበት ምግብ							
ማንኛውንም ስኳር፣ ማር፣ጣፋጭ፣ለስላሳ መጠጦች							

7.2.ባለፈዉ 24 ሰዓት ዉስት የተመገቡትን ምግቦች አስመልክቶ ለመጠየቅ የቀረቡ ጥቄዎች

ከዚህ በመቀጠል በትናንትናዉ እለት ቀንም ሆነ ማታ የተመገቡትን ጠንካራ፣ ለስላሳ ወይም ፈሳሽ ምግቦችን ልጠይቆት እፈልጋለዉ። ቤትም ሆነ ከቤት ዉጭ የበሉትን ማንኛዉም ምግብ፣ መጠጥ፣ ማጣፈጫ፣ ቅመሞች፣ መክሰስም ሳይቀር አንድታስታዉሱ ና እንድትነግሩኝ እፈልጋለዉ። በዚ ቃለ መጠይቅ ዉስጥ ትክክል ወይም ስህተት መልስ የለም። ጥያቄ ኣልት? ከሌሎትእንጀምር

<u>የአመጋገብመጠየቂያቅጽ: የ 24 ሰአት የምግብ ዝርዝር:</u> ከዚህ በመቀጠል በትናንትናዉ እለት ቀንም ሆነ ማታ የተመገቡትን/ የጠጡትን ደረቅ፣ ፈሳሽ እና ለስላሳ ምግቦችን በዝርዝር አጠይቆታለዉ።

የቃለ መጠይቁ አድራጊ ስም_____ ምግቡ የተበላበት ቀን_____

ለ መጠይቁ የተሰራበት ቀን፡ _____ የተጠያቂ መለያ ቁጥር _____ጾታ_____

ምግቡ የተበላበት ሰአት	ምግቡ የተበላበት ቦታ	የምግብ ወይም መጠጥ ዓይነት	የምግብ ዝርዝርና አሰራር	የተበላው መጠን በመለኪያ	የተበላው መጠን ግራም
ቁርስ					
ማቆያ					
ምሳ					
ማቆያ					
እረት					
ማቆያ					

7.2.1. የምግቦቹ ና ዉህዶቹ ገለፃ ፎርም፣ አሁን ደግሞ ከላይ የዘረዘሩልኝ ምግቦች የአበሳሰል ዘዴያቸዉ፣ ዉህዶቹና የዉህዶቹን መጠን፣ አይነትና ምን ያህል አንደተመገቡ በዝርዝር ይነግሩኛል።

የምግቡ/መጠጡ ዝርዝረ ና አይነቱ	የምግቡ/መጠጡ ገለፃና የአበሳሰል ዘዴ (ይህን መረጃ ለመሰብሰብ ዉህዶቹ፣ የዉህዶቹን አይነትና መጠን እና የአበሳሰል ዘዴዉን በጥልቁ ይጠይቁ)	የተዘጋጀው ምግብ መጠን (በመለኪያ)	የተበላዉ ምግብ መጠን (በመለኪያ)	ምግብ መጠን (በግራም)
	ዉህዶቹና የአበሳሰል ዘዴ፡ መጠናቸዉ (በመለክያ/ግራም)			
	ዉህዶቹና የአበሳሰል ዘዴ፡ መጠናቸዉ (በመለክያ/ግራም)			
	ዉህዶቹና የአበሳሰል ዘዴ፡ ና መጠናቸዉ (በመለክያ/ግራም)			
	ዉህዶቹና የአበሳሰል ዘዴ፡ ና መጠናቸዉ (በመለክያ/ግራም)			

701.	ስለተመጠጠነ የምግብ አመገጋብ ጥቅም ሰምተዉ/ተምረዉ ያዉቃሉ?	☐አዎ	☐አለዉቅም
702.	አዎን ካሉ ከየት እንደሆነ ይግለጹ?		
703.	በተመጠጠነ የምግብ አመገጋብ ለይ በቂ የሆነ የምክር አገልግሎት አግኝተዉ ያዉቃሉ?	☐አዎ	☐አለዉቅም
704.	የተለያዩ የምግብ ዓይነቶችን በቀን እንደይመገቡ የሚያደርጉ ሁኔታዎች አሉ ?	☐አዎ	☐የሉም
705.	አዎን ካሉ ምንድነዉ?	☐ የገቢ ሁኔታ ☐የአዉቀትና ሙያ ማነስ ☐ የባህል ተጽዕኖ ☐ ሌላ_____	
706.	የቤተሰብ ብዛት ምን ያህል ነዉ	ይገለፅ_____	
707.	አልኮል ጠጥተው ነበር?	☐አዎ	☐አይደለም
708.	ታመው ነበር?	☐አዎ	☐አይደለም
709.	አዎን ካሉ ህመሙ የአመጋገብህን/ሽን ሁኔታ ቀይሮ ነበር?	☐አዎ	☐አይደለም
710.	አዎ ከሆነ እነዴት ነዉ የቀየረዉ	☐ጨመረ	☐ቀነሰ
711.	የአመጋገብህ/ሽ ከድሮ ለየት ይለል?	☐አዎ	☐አይደለም
712.	እንዴት?	☐ ጨመረ	☐ቀነሰ
713.	የበኣል ቀን ነበረ?	☐አዎ	☐አይደለም
714.	የገብያ ቀን ነበረ?	☐አዎ	☐አይደለም
715.	የእረፍት ቀን ነበረ (ቅዳሜ/እዉድ) ?	☐አዎ	☐አይደለም
716.	የፆም ቀን ነበረ?	☐አዎ	☐አይደለም
717.	ምግብ ሳይመገቡ ዘለዉ ያዉቃሉ?	☐አዎ	☐አለዉቅም
718.	አዎን ካሉ የትኛዉን?	☐ቁርስ ☐ምሳ	☐እረት ☐ማቆያ
719.	መድሐኒት ወስደዋል	☐አዎ	☐አልወሰድኩም
720.	አዎን ካሉ ይግለጹ _____		

በአማርኛ ቋንቋ የተዘጋጀ የተለያዩ የሰዉነት ክፍሎች ልኬትና የላቦራቶሪ ዉጤቶች

የጠያቂዉ ስም_____**ቀን**_____

ተ፡ቁ_____	**የካርድ ቁ**_____	

የሰዉነት ክፍሎች ልኬትና የደም ግፊት		የመጀመሪያ ልኬት	የሁለተኛ ልኬት	አማካይ ልኬት
801	የክብደት መጠን [በኪሎግረም]?	_____	_____	
802	ክብደት ከቁመት አንፃር (በኪ፡ግረም/በሴ፡ሜ^2)?	_____	_____	
803	የቁመት መጠን [በሴንቲሜትር]?	_____	_____	
804	ከመቀመጫ በላይ የቁመት መጠን [በሴ፡ሜ]?			
805	የወገብ ዙሪያ ልኬት (በሴንቲሜትር)?	_____	_____	
806	የዳሌ ዙሪያ ልኬት (በሴንቲሜትር)?	_____	_____	
807	የአንገት ዙሪያ ልኬት (በሴንቲሜትር)?	_____	_____	
808	የደም ግፊት መጠን ሲስቶሊክ ናዲያስቶሊክ (በሚሊ ሜትር ሜሪኩሪ)?	_____ና_____	_____ና____	
809	የልብ ምት መጠን (በደቂቃ)?	_____	_____	
የባዮኢምፔዳንስ ዉጤቶች				
901	የሰውነት ስብ መጠን (በፐርሰንት)?	_____	_____	
902	የአጥነት ጡንቻ መጠን (በፐርሰንት)?	_____	_____	
903	የሆድ አካበቢ የስብ ክምችት መጠን?	_____	_____	
904	ባዮሎጅካል ዕድሜ (በዓመት)?	_____	_____	
በደም ውስጥ ያሉማዕድናት/ ኬሚካል የላቦራቶሪ ምርመራ ዉጤቶች				
101	ምግብ ሳይመገቡ በፊት በደም ውስጥ የነበረው የስኳር መጠን (በ ሚሊግረም/ዴሲሊትር)?	_____		
102	ግላይኬትድ ሄሞግሎቢን መጠን (በፐርሰንት)?	_____		
103	በደም ውስጥ ያለው የአጠቃላይ የኮሌስትሮል መጠን (በ ሚሊግረም/ዴሲሊትር)?	_____		
104	የትራይግላይሴራይድ መጠን (በ ሚግ/ዴሊ)	_____		
105	የከፍተኛ ዴንሲቲ ኮለስትሮል መጠን (በ ሚሊግረም/ዴሲሊትር)?	_____		
106	የዝቅተኛ ዴንሲቲ ኮለስትሮል መጠን (በ ሚሊግረም/ዴሲሊትር)?	_____		

Annex-VII: Trial Design and Study protocol

Effects of lifestyle modification counselling on anthropometrics and body composition in overweight/obese adults taking antiretroviral therapy: a randomized controlled trial

This study will be a two-arm randomized controlled trial (RCT) with equal allocation (1:1 ratio), to be conducted in ART clinics. The target population will include overweight and obese adults receiving antiretroviral therapy (ART).

Objectives

The primary objective will be to achieve and sustain at least a 3% weight loss within six months among overweight and obese ART clients. Participants in the intervention group will receive structured, personalized counselling focused on dietary changes, physical activity, and behavioral modifications. The control group will continue to receive routine ART care without structured lifestyle counselling during the study period, with counselling provided only after study completion.

Eligibility Criteria

Eligible participants will be adults aged 18 to 65 years on ART with a body mass index (BMI) of 25 kg/m² or higher who will consent to participate. Exclusion criteria will include pregnancy or breastfeeding, critical illness, severe mental disorders, or use of medications known to significantly affect weight.

Randomization and Sample Size

Participants will be randomized through simple randomization using a computer-generated sequence, with allocation concealed in simple random. Sample size calculations based on a 95% confidence level and 80% power, estimated 132 participants. This **resulted** in 66 participants per group.

Participant Flow and Contact Schedule

Participants in the intervention group will undergo an initial 50–60 minute face-to-face counselling session at baseline, followed by two telephone counselling sessions at months one and two, and a final weight and goal review at six months. After study completion, ongoing support will be offered. Control group participants will receive routine ART care without counselling during the study but will attend assessments at baseline and six months. They will receive full counselling after the study.

Intervention Group Protocol

Counselling will focus on three domains: dietary guidance, physical activity, and behavioral support. Dietary recommendations will emphasize a daily caloric deficit of 500 kcal, increased intake of whole grains (e.g., teff, barley), fiber-rich vegetables, fruits, legumes, lean proteins, and healthy fats, while limiting sugary drinks, processed grains, fried foods, and unhealthy fats. Physical activity guidance will encourage at least 150 minutes per week of moderate-intensity aerobic exercise such as walking or dancing, with the use of televised Ethiopian exercise programs recommended. Behavioral support will involve motivational interviewing, SMART goal setting, and use of food/activity logs. Counsellors will maintain a supportive tone, use

culturally adapted visual aids in Amharic, and follow a structured script offering clear actionable advice.

Control Group Protocol

The control group will continue routine ART services including clinical assessment and ART monitoring but will not receive lifestyle counselling during the study. Participants will attend baseline and six-month visits for weight and metabolic measurements. Full counselling will be provided after study completion to ensure equitable care.

Outcome Measures

The primary outcome will be the proportion of participants achieving at least 3% weight loss at six months. Secondary outcomes will include changes in waist circumference, BMI, physical activity, dietary patterns, and metabolic markers such as HDL cholesterol.

Data Collection and Monitoring

Trained personnel using standardized tools will collect data at baseline and six months. The principal investigator will oversee data quality and study monitoring.

Statistical Analysis

Analyses will follow the per protocol principle. Differences in means and proportions between groups will be tested using t-tests and chi-square tests, with regression models adjusting for relevant covariates as needed.

Counselling Tools and Resources

Counsellors in the intervention group will use Amharic-language brochures, visual cards depicting diet and exercise, food and activity logs, SMART goal templates, and checklists for remote counselling sessions.

Ethical Considerations

All participants will continue to receive standard HIV care. Informed consent will be obtained from each participant, and the control group will receive the full counselling intervention after six months to ensure fairness and ethical integrity.

Annex-VIII: Amharic version Brochure

1. ዉፍረት ምንድነዉ

ጤናማ ክብደት ማለት የሰዉነት ክብደት አመላከቾ መጠን (ቦዲ-ማስ እንዴክስ) ከ18.5-24.9ኪሎ ግረም/ሜትር ስኩዋር ሲሆን በሌላ አገላለጽ ደግሞ ጤናማ ክብደት ማለት የሆድ አካበቢ ቦርጭ ለወንዶች 101ሴንቲ ሜትርና ከዚያ በታች ሲሆን ለሴቶች ደግሞ 87 ሴንቲ ሜትርና ከዚያ በታች ነዉ።

ነገር ግን ጤናማ ያልሆነ የክብደት መጨመር ማለት የሰዉነት ክብደት መጠን (ቦዲማስ እንዴክስ) 25-29.9 ኪሎ ግረም/ሜትር ስኩዋር ሲሆን፡ ዉፍረት ማለት ማንኛዉም ሰዉ ክብደቱ 30 ኪሎግረም/ ሜትር ስኩርና ከዚያ በላይ ያለዉ ማለት ነዉ። ወይም በሌላ አገላለጽ ደግሞ ዉፍረት ማለት የሆድ አካበቢ ቦርጭ ለወንዶች 102ሴንቲ ሜትርና ከዚያ በላይ ሲሆን ለሴቶች ደግሞ 88 ሴንቲ ሜትርና ከዚያ በላይ ነዉ።

2. ከዉፍረት ጋር ተያይዞ የመከሰት ዕድል ያለቸዉ የጤና ስጋቶች

ዉፍረት ለተለያዩ የጤና ችግሮች ስጋት እንደሆነ ጥናቶች ያመለክታሉ። ለምሳሌ ያህል ለልብ ህመም፣ ለስትሮክ፣ ለደም ግፍት መጨመር፣ ለስኳር ህመም፣ ለመጥፎ ኮሌስቴሮል መጨመር፣ ለሀሞት ህመምና ለሀሞት ጠጠር፣ ለአጥንት ቁርጥማት፣ ለሪህ በሽታ ወይም ለዩሪክ አሲድ መጨመር፣ በእንቅልፍ ጊዜ የትንፋሽ መቋረጥ ችግር፣ ለመካንነት፣ ለእንደንድ የካንሰር ህመምና ለሌሎችም የጤና ችግሮች የመከሰት ስጋት አብዛኛዉን ጊዜ ከዉፍረት ጋር የመያያዝ ዕድለቸዉ ከፍ እንደሚል ጥናቶች ይጠቁማሉ።




3. ጤናማ የዉፍረት መቀነስ ጥቅሞች

ጤናማ የሆነ የዉፍረት/ ክብደት መቀነስ ማለት ከነበረዉ ዉፍረት 5 ፐርሰንት (5%) ክብደት መቀነስ ማለት ሲሆን ብዙ የጤና ጥቅም እንደለዉ ጥናቶች አረጋግጠዋል። ለምሳሌ የደም ግፍትን ለመቀነስ ፡ የስኳር መጠንን ወይም በስኳር የመያዝ ዕድልን ለመቀነስ፡ መጥፎ ኮሌስቴሮልን ለመቀነስ፡ የሀሞት ጠጠር ስጋትን ለመቀነስ፡ ለአጥንት ቁርጥማት ህመምን ለመቀነስ፡ የሪህ ህመምን ወይም ለዩሪክ አሲድ መጠንን ለመቀነስ፡ በእንቅልፍ ጊዜ የትንፋሽ መቋረጥ ችግርን ለመቀነስ፡ የደረት ህመምን ለመቀነስ፡ እንደንድ የካንሰር ህመሞችንና ሌሎችንም የጤና ስጋቶች ለመቀነስ ትልቅ ፈይደ አለዉ።

4. ጤናማ የሆኑ የዉፍረት መቀነሻ መንገዶች

የሚከተሉትን ጤናማ የዉፍረት መቀነሻ መንገዶችን በመጠቀም ከዉፍረት ጋር ተያይዘዉ የሚመጡትን የተለያዩ የጤና ዕክሎችን መከላከል ወይም መቀነስ ይቻላል።

4.1. አመጋገብን መስተከካል

ሀ. የኃይል ሰጪ ምግቦችን መጠን መቀነስ

የኃይል ሰጪ ምግቦችንመጠን ማለትም እንጄራ፡ የስንዴ ዳቦ፤ ቂጣ (የቦቆሎ፡ የስንዴ፡ የገብስ) እና አምባሻ መጠነቸዉን ቀንሶ መመገብ ብዙ የጤና ጥቅሞች እንደሉት ጥናቶች ያመለክታሉ፡ ለምሳሌ የእንሱልንን ክንዉን የመስተካከል፡ በስኳር የመያዝን ዕድል ይቀንሰል፡ ዉፍረትን የመቀነስ ዕድሉም ሰፊ ነዉ። እንደ አመጋገብዎ 1/3ኛ ወይም 1/4ኛን ድሮ ከሚመገቡት የሀይል ሰጪ ምግቦች መጠን ቀንሶ መመገብና የተቀነሰዉን የካሎሪ መጠን በምትኩ በሌሎች የምግብ ዓይነቶች ማለትም በፕሮቲን የበለጸጉ ምግቦች፡ በእትክልትና ፍራፍሬዎች በመተካት መመገብ ነዉ። ከልተፈተጉ እህሎች ወይም በፋይበር(በጭረት) ከበለጸጉ እህሎች የሚዛገጁ ምግቦችን መመገብ ዉፍረትን ከመቀነሱም በተጨማሪ ከተለያዩ የጤና እክሎች የመከለከል እድሉ ከፍ ያለ ነዉ። በተጨማሪ የአመጋገብ ሰዓትን መስተካከልና ከፍተኛ ካሎሪ ያለቸዉን ምግቦች ለምሳሌ ቾኮሌትን፡ ኬኮችን ደርቀዉ የተጠበሱ ምግቦች መጠነቸዉን በጠም ቀንሶ መመገብ ክብደትን ለመቀነስና ለመቆጠጠር አስተዋጽኦ አለቸዉ። እርሰዎም ይህንን የአመጋገብ ህይትን በመከተል ክብደትዎን/ ዉፍረትዎን መቀነስ ይችላሉ።

ለ. አትክልትና ፍራፍሬዎችን በተቻለ መጠን አብዝቶ መጠቀም፡

ቢቻል ቢቻል በቀን ቢያንስ 5 ጊዜ አትክልትንና ፍራፍሬዎችን መመገብ (ለምሳሌ፡- የተከፈለ ወይም አንድ ሙሉ ማንጎ፣ ብርቱካን፣ ፓፓዬ የመሰሰሉትንና አትክልትን ለምሳሌ ጎመን፡ ቆስጣ፡ ጥቅል ጎመን፡ አባባ ጎመን፡ ብሮኮሊ፡ ፎሶሊያ ወዘተ...)። እንደ ዓለመቀፍ የምግብ ፕሮግረም ጥቆማ መሰረት አትክልትና ፍራፍሬዎች በካሎሪ ዝቅተኛና ዉፍረትን ለመቀነስ በጠም አስፈላጊ ናቸዉ። በተጨማሪ አትክልትና ፍራፍሬዎች በንጥረ-ነገሮች የበለጸጉ ስለሆኑ የእንሱልን ስንፈትንና በስኳር የመያዝን እድል ይቀንሳሉ።በዉስጠቸዉ የሚገኘዉ የፋይበር(የጭረት) መጠን የጥገብ ስሜትን በመጨመር የምግብ ፍላጎትን ስለሚቀንሱ አመጋገብዎንለመመጠንም ጭምር ይረደሉ። ስለዚህ እርሰዎም ይህንን የአትክልትና ፍራፍሬ የአመጋገብ ስርዓትን በመከተል ክብደትዎን/ ዉፍረትዎን መቀነስ ይችላሉ።



ሐ. ጥረጥሬ(ፕሮቲን)እህሎችን አብዝቶ መመገብ

በቅባትና ስብ መጠን በጠም አነስተኛ የሆኑትንና በፕሮቲን የበለጸጉ ጥረጥሬ እህሎችን መመገብ ለምሳሌ፡- አተር፡ ባቄላ፡ ቦሎቄ፡ ወዘተ... በዉስጣቸዉ የፋይበር መጠን ከፍ ያለ በመሆኑ ለዉፍረት መቀነስ አስተዋጽኦ አላቸዉ። ስለሆነም እርስዎም የጥረጥሬ እህሎችን አመጋገብ በመዕድዎ አካተዉ በመመገብ ክብደትዎን/ ዉፍረትዎን መቀነስ ይችላሉ።



መ. ከመጠን ያለፈ ህይትን አልፈዉ የሚዘገጁ የሱቅ ምግቦች መጠንን መቀነስ/አለመጠቀም

በፋብሪካ በብዙ ህይቶች አልፋዉ የሚዘጋጁ ምግቦችን ለምሳሌ ነጭ ዳቦና ሌሎች ተያያዥ ምግቦችን መጠን

በእጅጉ መቀነስ ያስፈልጋል። በፋብሪካ በብዙ ሀደቶች አልፎ የሚዘጋጁ ምግቦች የካሎሪ መጠነቸዉ ብዙ ስለሆነ ዉፍረትን/ክብደትን ለመጨመር ትልቅ ዕድል ስላለቸዉ እነዚህን ምግቦች መቀነስ ዉፍረትንናሌሎችንም የጤና ችግሮችን ለመከላከል ትልቅ አስተዋጽኦ አለዉ።



ሰ. የስኳርና ስኳር ነክ ምግቦችና መጠጦች አጠቃቀም

እንደ አሜሪካ የልብ መህበር ምልከታ በቀን የስኳር መጠን ለወንዶች ከዘጠኝ የሻይ ማንኪያና ለሴቶች
ደግሞ ከስድስት የሻይ ማንኪያ እንደይበልጥ ይማከረል። በተጨማሪም ስኳርማና ሀይል ሰጪ መጠጦች፣ ኬኮች፣ ኩኪስ፣ አይስ-ክሬም፣ የጠፈጭ ፍረፍሬዎች መጠጥ፣ ካረሜላ ወዘተ...መጠነቸዉን በጠም ቀንሰዉ እንድመገቡ ይማከረል። ስለዚህ እርስዎም እነዚህን ጠፋጭ ምግቦችን በመቀነስ ክብደትዎን/ ዉፍረትዎንና ተያያዥ ችግሮችን መቀነስ ይችላሉ።



ሸ. ጠጣር የሆኑ ቅባቶችንና ከጠጠር ቅባቶች የሚሰሩ ምግቦችን መቀነስ/አለመመገብ

ጠጣር የሆኑ ቅባቶችን ማለትም ቅቤ፣ ሽኖ ለጋ፣ ሽድ ለጋ፣ ገርሊገይና፣ መሪጋሪን አለመጠቀምና በምትኩ ደግሞ ለጤና ጠቃም የሆኑ ፈሳሽ ዛይቶችን
(ሞኖአንሰቹሬትድና ፖሊ- አንሰቹሬትድ) ዛይቶችን ለምሳሌ አቮካዶ፣ የወይራና የለዉዝ ዛይቶችን ወዘተ መጠቀም። ጤናማ ቅባቶችን የዕለት ተዕለት አጠቃቀመችን ከ 20-35% ካሎሪ ብቻ የያዛ መሆን አለበት። ነገር ግን ከፍ ያለ የኮሌስቴሮል መጠንና የደም ቧንቧ ህመም ያለበቸዉ ሰዎች እላይ ከተገለጸዉ ካሎሪ በታች ቀንሰዉ እንድጠቀሙ ይማከረል። መጠነኛ የሆነ ስብና የቅባት ያለቸዉን የእንስሳትን ተዋጽኦ መመገብ ለምሳሌ የቀላል ቅባትማ አይብ፣ እርጎ፣ ቀላል ቅባትያለዉን/የተናጠ ወተትን መጠቀም ዉፍረትንና ሌሎችንም የጤና ችግሮችን ለመከላከል ትልቅ አስተዋጽኦ ስላለቸዉ እርስዎም እነዚህን ምግቦች መጠነቸዉን በመቀነስ/በመተዉ ክብደትዎን/ ዉፍረትዎን መቀነስ ይችላሉ።



4.2. የአካል ብቃትና ስፖርታዊ እንቅስቃሴዎችን መዘወተር

1. ሁሉንም ጠንካራ ተግባራት/ከባድ አካላዊ ጥረት የሚጠይቁ ስፖርታዊ እንቅስቃሴዎችን ማለትም ትንፋሽዎ ከተለመደው በላይ እንዲበዛ የሚየያደርጉ ለምሳሌ ከባድ እቃ ማንሳት፣ ኤሮቢክስ ወይም ብስኪሌት ማብረር ወዘተ...ሊጨምሩ ይችላሉ። በአንድ ጊዜ ቢያንስ ለ10 ደቂቃዎች ይሰሩአቸው የነበሩ አካላዊ ተግባራትን ጨምሮ መካከለኛ አካላዊ ተግባራት ማለትም አተነፋፈስዎን በተወሰነ ደረጃ ከተለመደው የበለጠ ፈጠን ያደርጋሉ። እንዲሁም ቀላል ጭነቶችን፣ ብስክሌት በመደበኛ ፍጥነት መንዳት፣ ወይም ጠረጴዛ ቴኒስ መጫወት ወዘተ...የተከመቸ ኃይል ለማቃጠል ጥቅማቸዉ ከፍ ያለ ነዉ።

2. ወይም መለስተኛ ጉልበት ስራ ብሎም ብዙ ትንፋሽ የማያስወጣ መጠነኛ ትኩረትና አንክሮ የሚፈልግ ስራ መስረት፣ ለምሳሌ ፈጠን ያለ ርምጃ፣ ቀለል ያለ እቃ መሸከም (ቢያንስ ለ 30 ደቂቃ በተከታታይ)። ከአንድ ቦታ ደርሶ ለመመለስ ቢያንስ 30 ደቂቃዎች የሚወስድ ጉዞን በእግር ወይም ቢስክሌት በመጠቀም መጓዝ፣ በቀጠይነት ለራስዎ በሚሰጡት የመዝናኛ ጊዜ ጉልበት የሚጠይቁ እና ትንፋሽ የሚያበዙ ስፖርቶችን ወይም የአካል ብቃት እንቅስቃሴዎችን ቢያንስ ለተከታታይ 30 ደቂቃዎች መድረግ (ለምሳሌ- እግር ኪስ መጫወት፣ ቴኒስ፣ ሩጫ፣ ፈጣን ዋና፣ ጂም፣በሙዚቃ የታገዘ የሰውነት ማጎልመሻ፣ ገመድ መዝለል) በቤት ወይም ከቤት ውጪ በሚያደርጉት መደበኛ እንቅስቃሴ ወይም የቤት ውስጥ ስራዎች መጠነኛ የትንፋሽና የልብ ምት መጨመር የሚያስከትሉ መካከለኛ አካላዊ እንቅስቃሴዎችን መስራት፣ የተከመቸ ኃይል ለማቃጠል ጥቅም አላቸዉ።

በተጨማሪ ከታች በተገለጹት የቴሌቪዥን ጣቢያዎች የሚተለላፉ የአካል ብቃትና ስፖርታዊ እንቅስቃሴዎችን ቢያንስ 30 ደቂቃዎች አብሮ በመስራት በሰዉነትዎ የተከመቸ ኃይል ለማቃጠልና ክብደትዎን/ ዉፍረትዎን ለመቀነስ ጤናዎትን ለመጠበቅ ከፍ ያለ አስተዋጽኦ አላቸዉ።

የቲቪ ፕሮግረም	የፕሮግረሙ ሰዓት፣ ጥዋት	የፕሮግረሙ ሰዓት፣ ማታ
ኢቲቪ መዝናኛ	12፡00-12፡30	12:30-1:00
ኢሳት ቲቪ	12፡00-12፡30	
ዋልታ ቲቪ	12፡00-12፡30	
አማራ ቲቪ	12፡00-12፡30	
አድስ ቲቪ	12፡00-12፡30	
ናሽናል ብሮድካስት (NBC)	12፡00-12፡30	
ኢቲቪ ዜና	12፡30-1፡00	
ፋና ቲቪ	12፡30-1፡00	
ኦብን ቲቪ (OBN)	12፡00-12፡30	
የልጆች ዓለም ቲቪ	12፡00-12፡30	



ጥያቄ ስኖርዎት (በ 0913175126 ይደዉሉ)

Adapted guidelines

- ✓ DASH diet, Mediterranean diet, AHA dietary guidelines;
- ✓ 5As (ask, assess, advise, agree, and assist) model

Annex-IX: Trial Design and Population protocol

Effects of lifestyle modification counselling on anthropometrics and body composition in overweight/obese adults taking antiretroviral therapy: a randomized controlled trial

This study will be a two-arm randomized controlled trial (RCT) with equal allocation (1:1 ratio), to be conducted in ART clinics. The target population will include overweight and obese adults receiving antiretroviral therapy (ART).

Objectives

The primary objective will be to achieve and sustain at least a 3% weight loss within six months among overweight and obese ART clients. Participants in the intervention group will receive structured, personalized counselling focused on dietary changes, physical activity, and behavioral modifications. The control group will continue to receive routine ART care without structured lifestyle counselling during the study period, with counselling provided only after study completion.

Eligibility Criteria

Eligible participants will be adults aged 18 to 65 years on ART with a body mass index (BMI) of 25 kg/m² or higher who will consent to participate. Exclusion criteria will include pregnancy or breastfeeding, critical illness, severe mental disorders, or use of medications known to significantly affect weight.

Randomization and Sample Size

Participants will be randomized through simple randomization using a computer-generated sequence, with allocation concealed in simple random. Sample size calculations based on a 95% confidence level and 80% power, estimated 132 participants. This **resulted** in 66 participants per group.

Participant Flow and Contact Schedule

Participants in the intervention group will undergo an initial 50–60 minute face-to-face counselling session at baseline, followed by two telephone counselling sessions at months one and two, and a final weight and goal review at six months. After study completion, ongoing support will be offered. Control group participants will receive routine ART care without counselling during the study but will attend assessments at baseline and six months. They will receive full counselling after the study.

Intervention Group Protocol

Counselling will focus on three domains: dietary guidance, physical activity, and behavioral support. Dietary recommendations will emphasize a daily caloric deficit of 500 kcal, increased intake of whole grains (e.g., teff, barley), fiber-rich vegetables, fruits, legumes, lean proteins, and healthy fats, while limiting sugary drinks, processed grains, fried foods, and unhealthy fats. Physical activity guidance will encourage at least 150 minutes per week of moderate-intensity aerobic exercise such as walking or dancing, with the use of televised Ethiopian exercise programs recommended. Behavioral support will involve motivational interviewing, SMART goal setting, and use of food/activity logs. Counsellors will maintain a supportive tone, use culturally adapted visual aids in Amharic, and follow a structured script offering clear actionable advice.

Control Group Protocol

The control group will continue routine ART services including clinical assessment and ART monitoring but will not receive lifestyle counselling during the study. Participants will attend baseline and six-month visits for weight and metabolic measurements. Full counselling will be provided after study completion to ensure equitable care.

Outcome Measures

The primary outcome will be the proportion of participants achieving at least 3% weight loss at six months. Secondary outcomes will include changes in waist circumference, BMI, physical activity, dietary patterns, and metabolic markers such as HDL cholesterol.

Data Collection and Monitoring

Trained personnel using standardized tools will collect data at baseline and six months. The principal investigator will oversee data quality and study monitoring.

Statistical Analysis

Analyses will follow the per protocol principle. Differences in means and proportions between groups will be tested using t-tests and chi-square tests, with regression models adjusting for relevant covariates as needed.

Counselling Tools and Resources

Counsellors in the intervention group will use Amharic-language brochures, visual cards depicting diet and exercise, food and activity logs, SMART goal templates, and checklists for remote counselling sessions.

Ethical Considerations

All participants will continue to receive standard HIV care. Informed consent will be obtained from each participant, and the control group will receive the full counselling intervention after six months to ensure fairness and ethical integrity.

Annex-X: Training Guide for Counsellors

Effects of lifestyle modification counselling on anthropometrics and body composition in overweight/obese adults taking antiretroviral therapy: a randomized controlled trial

A. Training Guide for Counsellors: Lifestyle Modification Intervention

Objective: To train ART clinic counsellors to deliver a structured lifestyle counselling intervention aimed at achieving a minimum 3% weight loss over 6 months through diet modification, physical activity, and behavioural change.

***1. Intervention Overview**

- **Target:** ART clients with elevated weight/BMI or metabolic risk.
- **Goal:** At least 3% reduction in baseline weight within 6 months.
- **Method:** One face-to-face counselling session (50-60 minutes) and at least two phone follow-ups (20-30 minutes each).
- **Language:** Amharic, supported with brochures, pictures, and handouts.

***2. Counselling Protocol for Face-to-Face Session (50-60 minutes)**

1. Welcome and Rapport Building

- Greet the client warmly.
- Explain that the session is meant to support their health.
- Emphasize confidentiality and a non-judgmental approach.

2. Assess Eating and Physical Activity Patterns

- Ask the client to describe what they usually eat for breakfast, lunch, and dinner.
- Ask how often they eat snacks and what types.
- Ask about current physical activity, including walking, housework, job-related activities.
- Identify any barriers to healthy eating or exercising (e.g., time, money, energy).

3. Explain the Purpose and Goal of the Intervention

- Describe the health risks of overweight and the benefits of even modest weight loss.
- Clearly explain the goal: "We aim to help you lose at least 3% of your body weight over 6 months."
- Use charts or visuals to demonstrate what a 3% weight loss would look like.

4. At Baseline and 6-Month Visits:

- Describe information such weight, body composition, waist circumference, and dietary habits measurement at baseline and at the end of six months to help us understand health patterns in people living with HIV.

5. Diet and Nutrition counselling

- Explain caloric reduction target (~500 kcal/day).
- Emphasize balanced meals that include:

✓ **Whole grains:** barley, teff (injera), oats and others.

✓**Vegetables:** collard greens (gomen), spinach, cabbage, carrots, green beans, pumpkin and others.

- ✓ **Fruits:** bananas, papaya, oranges, mangoes, guava, apples.
- ✓ **Fibre-rich local foods:** Moringa oleifera leaves, lentils, chickpeas, beans, flaxseeds.
- ✓ **Lean proteins:** boiled eggs, grilled chicken, legumes, lentils, low-fat milk.
- ✓ **Healthy fats:** avocado, groundnut paste in moderation, flaxseed oil, sunflower oil.

✓ Advise avoiding sugary drinks, fried foods, processed snacks, refined grains, and saturated fats.

✓ Recommend drinking clean water instead of sugary drinks.

- Avoid or reduce:
  - ✓ Sugary snacks and drinks.
  - ✓ Fried or greasy foods.
  - ✓ Processed foods (packaged biscuits, instant noodles).
  - ✓ White bread, pasta, and refined grains.
- Demonstrate portion control using pictures or plates.

6. Physical Activity Guidance

- Recommend at least 150 minutes of moderate activity per week.
- Give examples: brisk walking, dancing, sweeping, or using the TV-based exercise program.
- Help the client identify times in the week they could exercise.
- Encourage walking instead of transport when possible.
- Emphasize reducing sedentary time (e.g., TV watching, long sitting).

7. Behaviour Change and Motivation

- Ask the client what motivates them to lose weight (e.g.,nfeel better, avoid illness).
- Encourage small steps and celebrate existing good habits.
- Identify what has worked or failed in past weight-loss attempts.
- Build confidence: "You don't have to change everything at once—small steps matter."

8. Goal setting

- Work with the client to set 2–3 specific and realistic goals.
  - Example goals:
    - Replace sugary drinks with water.
    - Walk 30 minutes three times this week and
    - Increase 30 minutes walking to at least for 5 days (moderate to vigorous intensity).
    - Add a vegetable and fruits to each mealtime as much as possible.

9. Provide Educational Materials

- Distribute the Amharic-language brochure with visuals.
- Explain how to use the food and activity log.

10. Plan for Follow-Up

- Schedule two phone calls in the coming two months.
- Remind the client that support is available and progress will be reviewed.

***3. Phone Follow-Up Protocol (20–30 minutes)**

Key Steps:

- Greet and check in on well-being.

- Ask about progress toward the goals.
- Reinforce healthy behaviours.
- Address any new or ongoing challenges.
- Help revise or set new goals if needed.
- Encourage continued effort and schedule next contact.

***4. Do's and Don'ts for Counselling**

Do:

- Speak in clear, respectful Amharic.
- Be patient and supportive.
- Celebrate small successes.
- Use visuals and examples.
- Personalize advice.

Don't:

- Do not blame or criticize.
- Do not recommend extreme or unsafe practices.
- Do not ignore questions or concerns.

***5. Tool & Materials to Provide Participants**

- Amharic-language brochure (with pictures).
- SMART goal-setting card.
- Food & activity log.
- Physical activity flyer (TV-based exercise guidance).

***6. Training for Counsellors (for Trainers)**

- Practice delivering each counselling item.
- Use role-play scenarios to build confidence.
- Demonstrate portion visuals and exercise examples.
- Assess through mock sessions and group feedback.

B. <u>Training Guide for Counsellors: Control Group</u>

Although the control group does not receive structured lifestyle counselling during the study period, counsellors must ensure consistency, ethical conduct, and clear communication at all participant contacts.

1. Role of Counsellor in Control Group

- Provide standard ART services only (e.g., clinical check-ups, medication adherence support).
- Maintain the same level of attention and respect as given to the intervention group.
- Refrain from offering any lifestyle modification advice related to diet, physical activity, or weight loss until after the final assessment.

2. Key Instructions

- **At Baseline and 6-Month Visits:**
  - We will collect information such as your weight, body composition, waist circumference, and dietary habits at baseline and at the end of six months to help us understand health patterns in people living with HIV. This data is used for research

purposes only and will not be used to guide individual treatment at this stage. Some participants may receive additional health guidance as part of the study.

- Avoid offering any lifestyle guidance that may influence behaviour.
- Maintain neutral tone and avoid bias toward intervention group messages.
- Reassure participants that full lifestyle counselling will be provided after study completion.

- **After Final Assessment:**
  - Offer full counselling intervention using the same tools and materials used for the intervention group (e.g., face-to-face session, Amharic brochure, and diet and activity guidance).

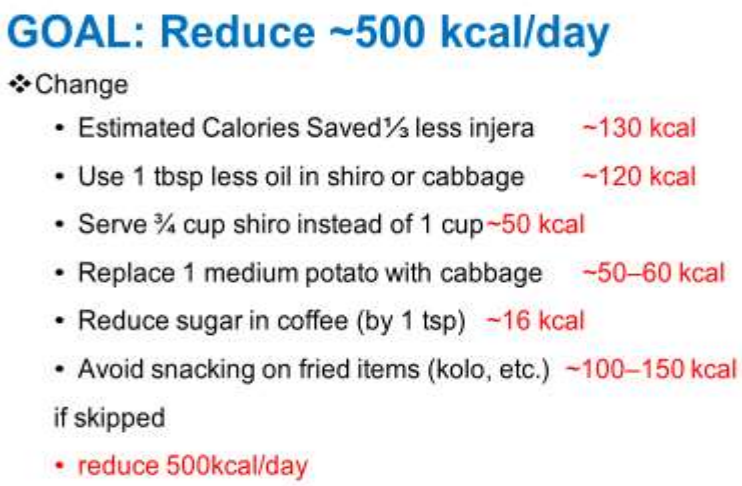
3. Ethical Considerations

- Obtain informed consent explaining the delayed counselling.
- Ensure confidentiality, dignity, and non-discrimination for all participants.
- Document all interactions and maintain clear communication with the study team.

4. Monitoring & Quality Control

- Supervisors will regularly check adherence to the control group protocol.
- Any deviation must be reported to the study coordinator.

Some examples of 500kcal reduction counselling



GOAL: Reduce ~500 kcal/day….

Food Item

- InjeraEat ¾ of large injera instead of whole ~100 kcal
- Lentil stew Serve ¾ cup instead of 1 cup ~50 kcal
- Tikil gomen: Use 1 tsp less oil ~40 kcalCoffee (2 cups)
- Use 1 tsp sugar per cup instead of 2 tsp ~16 kcalSkip snack bread
- Avoid 1 small slice of white bread ~100 kcal
- Avocado Eat ½ instead of whole fruit (large) ~100 kcal
- Total ~522 kcal save

GOAL: Reduce ~500 kcal/day….

- Tibs (100g → 50g) Smaller portion ~150 kcal
- Oil reduction 1 tbsp less during cooking ~120 kcal
- Injera (¾ instead of full) Portion cut ~100 kcal
- No bread or potato Skip 1 slice or half potato ~80–100 kcal
- Less sugar in tea 1 tsp less ~16 kcal
- Total ~500–530 kcal save

GOAL: Reduce ~500 kcal/day….

- Macaroni/pasta Serve 1 cup instead of 1½ cups~100 kcal
- Tibs Use 1 tbsp less oil during preparation ~120 kcal
- Sweet potato Eat ½ medium potato instead of full ~60 kcal
- Tea (2 cups) Skip sugar or use just 1 tsp total ~16 kcal
- No juice Skip 1 cup organic juice (unsweetened)~100–120 kcal
- Small injera use smaller size or cut portion ~100 kcal
- Total ~510–530 kcal save

Annex-XI: food items and portions (Pictorial and photograph show)



(only) = 295 g	bread = 100 g	bread = 110 g	1 glass of homemade mixed fruit juice= 250 g
			

1 medium ladle shiro stew = 100 g	1 average adult handful (efign in Amharic) of roasted beans (qollo)=30 g	1 medium ladle lentil stew = 125 g	1 average adult handful (efign in Amharic) of germinated beans (beqolt) = 45 g
			

1 medium-sized banana = 150 g	1 medium-sized orange = 200 g	1 medium-sized avocado = 150 g	1 medium-sized mango = 250 g
			
1 medium-sized lemon = 35 g	1 medium-sized slice of papaya = 75 g	1 medium-sized slice of watermelon = 150 g	1 medium-sized slice of pineapple = 35 g
			

1 medium-sized spoon of salad = 35 g	1 medium-sized scoop of cooked kale = 35 g	1 medium-sized scoop of mixed cooked vegetables = 25 g
		

1 average handful of groundnuts = 21	1 average handful of roasted sunflowers = 15 g	Sun flower juice mixed with pieces of injera (*Yesuf fetfet*) = 25 g	1 teaspoon of peanut butter = 10 g
			

1 medium-sized ladle of meat stew = 85 g	1 medium-sized ladle of meat + kalo stew = 50 g	1 medium sized fried fish = 300 g	1 medium-sized fish gulash = 80 g
			

1 medium-sized boiled egg = 50 g	2 medium-sized scrambled eggs = 50 g
	

1 Tablespoon of oil = 10 g	1 Tablespoon of spread butter = 15 g
	

1 glass of milk = 200 g	1 cup of yogurt = 350 g	1 Tablespoon of cottage cheese = 25 g
		

1 teaspoon of sugar = 4 g	1 medium-sized cake = 150 g	1 medium-sized glass of Coca Cola/soft drink = 340 g	1 medium-sized cookie = 9 g
			
1 medium-sized doughnut = 144 g	1 medium-sized sweet = 5 g	1 teaspoon of honey = 5 g	1 medium ladle of potato stew = 80 g
			

1 time use sunflower paste to prepare suf fitfit =25 g	1 medium ladle fish stew = 80 g	1 teaspoon of honey = 5 g
		

1 medium-sized sized banana = 150 g	1 medium-sized orange = 200 g	1 medium sized avocado = 150 g	1 medium-sized mango = 250 g
			
1 medium-sized lemon = 35 g	1 medium-sized slice of papaya = 75 g	1 medium slice of watermelon =150 g	1 medium slice of pineapple = 35 g
			
1 bottle of beer = 225 g	1 *birile tej* = 300 g	1 glass of wine = 220 g	1 glass of *tela* = 230 g
			



















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Annex-XII: Trial registration

Thai Clinical Trials Registry
www.thaiclinicaltrials.org

TCTR ID : TCTR20240905007

OTHER ID :

Overall Recruitment Status : Completed **(No Results)**

Retrospective registration
This protocol was registered after enrollment of the first participant.

Tracking Information

First Submitted Date :	03 September 2024
First Posted Date :	05 September 2024
Last Update Posted Date :	05 September 2024

Title

Public Title :	The effects of lifestyle counselling on anthropometric and body composition parameters in overweight/obese adults with HIV receiving first-line antiretroviral therapy: A randomized controlled trial
Acronym :	No Data
Scientific Title :	The effects of lifestyle counselling on anthropometric and body composition parameters in overweight/obese adults with HIV receiving first-line antiretroviral therapy: A randomized controlled trial
Sponsor ID/ IRB ID/ EC ID :	CNS-IRB
Registration Site :	Thai Clinical Trials Registry
URL :	https://www.thaiclinicaltrials.org/show/TCTR20240905007
Secondary ID :	No Secondary ID

Ethics Review

1. Board Approval :	Submitted, approved
Approval Number :	IRB?07/14/2022
Date of Approval :	19 September 2022
Board Name :	CNS-IRB
Board Affiliation :	Addis Ababa University
Board Contact :	Business Phone : 111239472 Ext. No Data Business Email : dean_cns@aau.edu.et Business Address : Ethiopia

Sponsor

Source(s) of Monetary or Material Supports :	Addis Ababa University
Study Primary Sponsor :	Addis Ababa University
Responsible Party :	Name/Official Title : Addis Ababa University Organization : Addis Ababa University Phone : 111239472 Ext. No Data Email : dean_cns@aau.edu.et
Study Secondary Sponsor :	No Study Secondary Sponsor

Protocol Synopsis

Protocol Synopsis :	The intervention group will receive counseling from trained counselors on improving an individual's level of physical activity and dietary habits including cognitive behavioral therapy. However, the participants in the control group will not receive formal dietary or exercise counseling from counselors.

URL not available

Health Conditions

Health Condition(s) or Problem(s) Studied :	overweight or obesity
Keywords :	lifestyle intervention, HIV, overweight, obesity, antiretroviral therapy

Eligibility

Inclusion Criteria :	1. The study were enrolled PLWH with overweight or obese, aged 18-65 years 2. They had started combination antiretroviral therapy following the implementation of the test-and-treat strategy in Ethiopia and received antiretrovirals for at least 12 months 3. Maintained viral suppression, and were free of opportunistic infections during the intervention.

This document was created on 11 February 2025 at 14:14 (GMT+7).

4. Eligible participants who had a baseline physical activity level of less than 600 metabolic equivalents in minutes per week

Gender : Both

Age Limit : Minimum : 18 Years Maximum : 65 Years

Exclusion Criteria : 1. The participants who had undergone formal dietary or physical activity counselling or engaged in organized nutritional and physical activity programs at baseline of the study.
2. Individuals with a history of pulmonary or cardiac complications, neurological problems, or musculoskeletal disorders were excluded from the study.
3. The individuals with confirmed thyroid disease, uncontrolled hypertension, physical conditions that restrict the ability to engage in physical activity, pregnancy at any point during the study, and those with chronic liver and/or renal diseases.
4. Additionally, participants who are undergoing lent or other fasting practices at any point during the study and those failing to meet the inclusion criteria were also excluded.

Accept Healthy Volunteers : No

Status

Overall Recruitment Status : Completed

Key Trial Dates

Study Start Date (First enrollment) : 05 January 2023	Indicate Type : Actual
Completion Date (Last subject, Last visit) : 30 April 2024	Indicate Type : Actual
Study Completion Date : 10 June 2024	Indicate Type : Actual

Design

Study Type : Interventional

Primary Purpose : Prevention

Study Phase : Phase 0

Intervention Model : Parallel

Number of Arms : 2

Masking : Open Label

Allocation : Randomized

Control : No treatment / Standard of care

Study Endpoint Classification : N/A

Sample size

Planned sample size : 132

Actual sample size at study completion : 116

Intervention Arm 1

Intervention name : counselling group

Intervention Type : Experimental

Intervention Classification : Behavioral

Intervention Description : The primary outcome of the study was the change in body weight and body composition at 6 months. Weight change was assessed as both the amount lost from baseline and the percentage of baseline body weight lost. We anticipated that the intervention group would achieve at least a 3 percent reduction in overall body weight compared with the initial measurements after six months. Moreover, the clinical measures and lifestyle counselling were conducted by trained ART staff, suggesting that, hypothetically, if this counselling was provided by ART staff, it could lead to weight loss and improved body composition among overweight/obese PLWH on ART, which may be helpful in primary healthcare settings with limited resources. The structured intervention included a 50 to 60 minute face to-face counselling session on lifestyle changes, which was conducted at baseline after all the study measurements were completed. Each participant received nutrition counselling from a trained counsellor, who utilized motivational interviewing techniques overseen by the principal investigator. The counselling sessions focused on plant-based foods, whole grains, fibre, lean protein, and low-fat dairy while advising a reduction in saturated fat, added sugar, and high-calorie, sugary foods. Strategies included incorporating fibre-rich local foods and increasing daily fruit and vegetable consumption to support weight reduction. The counsellor recommended choosing foods with a low to medium glycaemic index and high fibre content, limiting fatty foods, and reducing both saturated and total fat intake. The participants were also guided to avoid excessive eating, refined grains, fast food, and junk food. With respect to physical activity, participants were advised to increase their energy expenditure by engaging in either 150 to 300 minutes of moderate-intensity exercise per week, such as brisk walking, swimming, dancing, gardening, aerobics, or biking, or 75 to150 minutes of

vigorous-intensity exercise, including running, aerobic dancing, or cycling at speeds of 15 km/h or faster. Alternatively, a combination of both exercise types is recommended.

Intervention Arm 2

Intervention name : control group

Intervention Type : No Intervention

Intervention Classification : No treatment

Intervention Description : the CG did not receive structured nutritional, behavioral or exercise counselling from study-trained counsellors. Instead, participants in the CG received only routine assisted reality, antiretroviral treatment care services.

Outcome

Primary Outcome

1. Outcome Name : weight loss and change in body composition

Metric / Method of measurement : by using previously validated bioelectrical impedance(BIA). BIA was employed via an Omron Body Composition Monitor with Scale (Omron HBF-514C analyzer, Omron healthcare Inc., Japan)

Time point : at baseline and after 6 months

Secondary Outcome

1. Outcome Name : at least 3% weight loss

Metric / Method of measurement : percent weight loss: ([weight at 6 months minus weight at baseline]/weight at baseline)x100

Time point : at baseline and after 6 months

Location

Section A : Central Contact

Central Contact	First Name : Agete Tadewos	Middle Name :	Last Name : Hirigo
	Degree : MSc, PhD candidate	Phone : 0913175126 Ext. : No Data	Email : agetetadewos@yahoo.com
Central Contact Backup	First Name : Zelalem	Middle Name :	Lastname : Debebe
	Degree : MD, dietetics	Phone : 0920032918 Ext. : No Data	Email : zelalem.debebe@aau.edu.et

Section B Facility Information and Contact

1.	Site Name : Hawassa		
	City : Hawassa	State/Province : Sidama	Postal Code : 1560
	Country : Ethiopia	Recruitment Status : Completed	
Facility Contact	First Name : Ayalew	Middle Name :	Last Name : Astatkie
	Degree : PhD	Phone : 0911739694 Ext. : No Data	Email : ayalewastatkie@gmail.com
Facility Contact Backup	First Name : Zelalem	Middle Name :	Last Name : Debebe
	Degree : MD, Dietetics	Phone : 0920032918 Ext. : No Data	Email : zelalem.debebe@aau.edu.et
Investigator Name	First Name : Agete Tadewos	Middle Name :	Last Name : Hirigo
	Degree : MSc	Role : Principal Investigator	

Section C : Contact for Public Queries (Responsible Person)

First Name : Agete Tadewos	Middle Name :	Last Name : Hirigo
Degree : MSc, PhD candidate	Phone : 0913175126 Ext. : No Data	Email : agetetadewos@yahoo.com
Postal Address : Hawassa		
State/Province : Hawassa	Postal Code : 1560	
Country : Ethiopia	Official Role : Study Principal Investigator	
Organization Affiliation : Hawassa University		

Section D : Contact for Scientific Queries (Responsible Person)

First Name : Ayalew	Middle Name :	Last Name : Astatkie
Degree : PhD	Phone : 0911739694 Ext. : No Data	Email : ayalewastatkiee@yahoo.com
Postal Address : Hawassa		
State/Province : Sidama region	Postal Code : 1560	
Country : Ethiopia	Official Role : Study Principal Investigator	
Organization Affiliation : Hawassa University		

Summary Results

Date of posting of results summaries :	Summary results not yet available
Date of first journal publication of results :	Not yet published

Deidentified Individual Participant-level Data Sharing

Plan to share IPD :	Yes
Plan description :	after completing the data analysis the results will be presented for antiretroviral clinic workers, Addis Ababa university and manuscript will be submitted to reputable journal for publication

Publication from this study

MEDLINE Identifier :	not published
URL link to full text publication :	No Data

This document was created on 11 February 2025 at 14:14 (GMT+7).

COLLEGE OF NATURAL & COMPUTATIONAL SCIENCES

Addis Ababa University

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Ref.No. CNCSDO/153/15/2022
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Date September 19, 2022
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To Whom It May Concern

The College of Natural & Computational Sciences Institutional Review Board (**CNS-IRB**) Committee in its meeting held on **10/09/22 Minute No. IRB/07/14/2022** has examined the project proposal entitled "Changes in body weight, body composition and cardiometabolic risks and the effect of intensive counseling among HIV-positive adults receiving antiretroviral regimens at Hawassa City administration, Sidama Regional State, Ethiopia'' **by Agate Tadewos** from the Addis Ababa University.

The proposal is approved for implementation for one year, effective September 10, 2022.

With regards,

Addisalem Abathun, (PhD)
Dean, College of Natural & Computational Sciences
Addis Ababa University

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Please Quote our reference number in you correspondence

"Examine all things; hold fast that which is good"

"ሁሉን መርምሩ መልካሙን ያዙ"