American Journal of Preventive Cardiology 20 (2024) 100888

Contents lists available at ScienceDirect

American Journal of Preventive Cardiology

journal homepage: www.journals.elsevier.com/american-journal-of-preventive-cardiology

State-of-the-Art Review

# Optimizing cardiometabolic risk in people living with human immunodeficiency virus: A deep dive into an important risk enhancer

Elizabeth A. Kobe [a,*], Aarti Thakkar [a], Sarina Matai [b], Esra Akkaya [c,d], Neha J. Pagidipati [a,c,e], Robert W. McGarrah [a,c,d], Gerald S. Bloomfield [a,e,f], Nishant P. Shah [a,c,e]

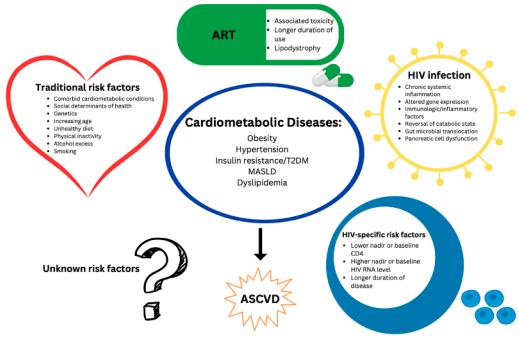
[a] Duke University Hospitals, 2301 Erwin Road, Suite 7400, Cubicle 13, Durham, NC 27710, USA
[b] Raleigh Charter High School, 1307 Glenwood Ave, Raleigh, NC 27605, USA
[c] Duke University School of Medicine, 8 Searle Center Dr, Durham, NC 27710, USA
[d] Duke Molecular Physiology Institute, 300 N Duke St, Durham, NC 27701, USA
[e] Duke Clinical Research Institute, 300 W Morgan St, Durham, NC 27701, USA
[f] Duke Global Health Institute, 310 Trent Dr, Durham, NC 27710, USA

ARTICLE INFO

*Keywords:*
Cardiometabolic diseases
Human immunodeficiency virus
Atherosclerosis
Primary prevention
Secondary prevention
Risk modification

ABSTRACT

Effective antiretroviral therapy (ART) is now nearly ubiquitous. However, the survival benefits conferred with ART contribute to an aging human immunodeficiency virus (HIV) population and increased risk of chronic diseases, like atherosclerotic cardiovascular disease (ASCVD). Furthermore, HIV is a known risk enhancer of ASCVD and acknowledged as such in the current 2018 AHA/ACC Blood Cholesterol guidelines [1]. This makes cardiovascular risk factor identification and modification among people living with HIV (PLWH) of increasing importance to prevent cardiovascular events. In this review, we aim to summarize the epidemiology and pathogenesis of how HIV is linked to atherogenesis and to discuss cardiometabolic risk factor modification specific to PLWH, covering obesity, hypertension, insulin resistance, metabolic dysfunction-associated steatotic liver disease, and dyslipidemia.




**Central illustration.** Cardiometabolic and atherosclerotic risk factors among PLWH. Abbreviations: ART, antiretroviral therapy; HIV, human immunodeficiency virus; T2DM, type 2 diabetes mellitus; MASLD, metabolic dysfunction-associated steatotic liver disease; RNA, ribonucleic acid; ASCVD, atherosclerotic cardiovascular disease.

## 1. Introduction

With the increased effectiveness and availability of antiretroviral therapy (ART), human immunodeficiency virus (HIV) has made an epidemiological transition to a chronic disease. Globally, there are more than 35 million people living with HIV (PLWH). This improvement in survival has been matched with a rise in non-communicable illnesses, particularly cardiovascular disease.

In a 2018 meta-analysis of 793,635 PLWH and a total of 3.5 million person-years of follow-up, the global prevalence of cardiovascular disease attributed to HIV nearly tripled over the past 26 years, with a crude rate of ASCVD of 61.8 per 10,000 person-years [2]. This increased prevalence varies regionally, with the largest portion of disability-adjusted life-years lost in sub-Saharan Africa and the Asia Pacific. Further, PLWH have an increased risk of myocardial infarction compared to people without HIV, with a relative risk ranging from approximately 50% to doubling of risk [3–6]. Not to mention, PLWH are at increased risk of ischemic stroke, heart failure, and sudden cardiac

* Corresponding author.
*E-mail address:* elizabeth.kobe@duke.edu (E.A. Kobe).

https://doi.org/10.1016/j.ajpc.2024.100888
Received 4 July 2024; Received in revised form 13 October 2024; Accepted 27 October 2024
Available online 28 October 2024

death compared to people without HIV [7–11].

The pathophysiology behind atherosclerosis development and progression in HIV is multifactorial, including HIV and ART-specific effects, co-infections, psychosocial factors, disparities in care, and metabolic comorbidities. For one, HIV causes chronic immune activation and inflammation [12,13]. Elevated biomarkers of inflammation (i.e., interleukin-6, tumor necrosis factor receptors α-1 and α-2), monocyte activation markers (i.e., soluble CD163 and CD14), and coagulation activity (i.e., D-dimers) are associated with increased vessel inflammation, endothelial dysfunction, and atherosclerotic plaque formation, instability, and risk of rupture [14–18]. This immune response may be further stimulated by co-pathogens, such a cytomegalovirus [19]. Even in the setting of sustained HIV viral suppression, PLWH have increased risk of ASCVD compared to those without HIV [3]. Certain ART, such as protease inhibitors [20,21], have also been associated with elevated ASCVD risk, as have social determinants of health, including disparities in care access, stigmatization, social support, neurocognitive decline, and substance use, particularly smoking [22–29]. Finally, HIV and certain ART are both implicated in the pathogenesis of metabolic comorbidities. Like the general population, cardiometabolic comorbid conditions such as hypertension, obesity, dyslipidemia, insulin resistance, and metabolic dysfunction-associated steatotic liver disease are important ASCVD risk factors, making the interplay of HIV, its associated factors, and cardiovascular diseases quite complex.

Despite this, few randomized clinical trials exist within the cardiovascular and cardiometabolic space investigating cardioprotective strategies and thresholds for initiating cardiovascular disease prevention strategies among PLWH. The Strategies for Management of Antiretroviral Therapy (SMART) Study Group was the first to investigate the impact of disease control through episodic or continuous antiretroviral therapy and cardiovascular disease, finding increased risk among those with low CD4+ counts [30]. The Randomized Trial to Prevent Vascular Events in HIV (REPRIEVE) investigated the use of statins to prevent atherosclerotic cardiovascular disease among PLWH who are at low-to-moderate risk for cardiovascular events, demonstrating a meaningful risk reduction among those receiving pitavastatin [31]. Given the relative lack of adequately powered randomized controlled trials among PLWH, our present understanding of cardiovascular disease prevention and treatment in HIV largely relies on large observational studies.

Even so, recent cohort studies, meta-analyses, and guidelines have highlighted the growing prevalence of cardiometabolic diseases among PLWH and recognized HIV as a cardiovascular risk enhancer. Current guidelines often vary in their screening and management recommendations, as data is constantly evolving and often derived via casual inference from retrospective cohort studies. This review aims to summarize the pathogenesis, epidemiology, risk factors, major guideline recommendations, and when relevant clinical trial data for specific cardiometabolic diseases associated with ASCVD among PLWH (Central Illustration). While existing guidelines such as the United States Department of Health and Human Services Panel provide detailed guidance on dyslipidemia management among PLWH specifically, we provide a more holistic approach covering a spectrum of cardiometabolic issues in HIV. We also offer our own clinical approach to managing cardiometabolic diseases among PLWH in an effort to better optimize ASCVD risk.

## 2. Obesity and weight gain

### 2.1. Pathogenesis

While uncontrolled HIV is associated with a state of catabolism and wasting, there has been a rising proportion of overweight and obese individuals living with HIV since the introduction of ART [32–34]. HIV and ART promote adipose tissue deposition via increased systemic inflammation and altered gene expression, immunologic regulation, and reversal of the catabolic state of uncontrolled viremia [35–42].

### 2.2. Epidemiology

Like the general population, the prevalence of overweight and obesity among PLWH appears to be increasing over time. An evaluation of prospective data from the U.S. Military HIV Study (1985–2004) found a near two-fold increase in overweight (25% versus 41%) and near four-fold increase in obesity (3% versus 12%) at the time of HIV diagnosis from 1985–1990 compared to 1996–2004 [32], rates of increase that appear quicker than the general population [43]. Similarly, using data from the North America AIDS Cohort Collaboration on Research and Design (NA-ACCORD) and the United States National Health Nutrition Examination Survey (NHANES) on 14,084 PLWH who started ART from 1998–2010, the prevalence of obesity at ART initiation increased from 9% to 18% over the same timeframe [33]. In addition to increased overweight and obesity prevalence at time of HIV diagnosis, there seems to be a temporal trend linked with increased ART uptake. Among the NA-ACCORD and NHANES population, after 3 years of ART, 22% of those with normal body mass index had become overweight and 18% of those overweight at baseline had developed obesity [33]. Similarly, among 681 ART-naïve PLWH (2000–2008), 20% of individuals with normal starting body mass index developed overweight or obesity after 24 months of ART [34]. Finally, in the Swiss HIV Cohort Study population, the prevalence of overweight and obesity increased from 13% (12% overweight, 1% obese) in 1990 to 38% (29% overweight, 9% obese) in 2012, coinciding with an increase in ART use from 38% to 92% [44].

### 2.3. Factors associated with increased risk of weight gain, overweight, and obesity

Factors associated with increased weight gain among PLWH include lower body mass index at diagnosis [32], African American race [44–48], female sex [46–50], and comorbid conditions such as hypertension [50] and diabetes [50]. HIV-specific factors include lower baseline or nadir CD4 count [44–46,50,51], increasing CD4 count over time [32], higher baseline HIV RNA level [46,50], decreasing HIV RNA level over time [32], longer HIV and ART duration [32,48], and more recent year of diagnosis [32].

While the initiation of ART is a well-cited risk factor for the development of overweight or obesity, this seems to be a class and medication-specific effect. Studies examining older nucleoside reverse transcriptase inhibitors (NRTIs) and non-nucleoside reverse transcriptase inhibitors (NNRTIs) have not been associated with weight gain [40,44], whereas more recent studies investigating integrase strand transfer inhibitors (INSTIs) have been associated with weight gain, particularly dolutegravir (DTG) [40,50–56]. Tenofovir alafenamide (TAF)-containing regimens, although a NRTI, are associated with higher weight gain compared to other NRTI-based regimens [40,42,56]. The combination of INSTI and TAF is associated with greater weight gain than INSTI or TAF alone [56,57]. The findings of these cohort studies were confirmed with a systematic review and meta-analysis of 73 studies examining weight gain associated outcomes between various ART-based therapies. In this meta-analysis, Kanters et al. demonstrated DTG-based regimens had higher weight gain than efavirenz (EFV), elvitegravir/cobicistat (EVG/c), and rilpivirine (RPV)-based regimens and similar weight gain to raltegravir (RAL) and bictegravir (BIC) [46]. Further, the analysis found that TAF promoted higher weight gain compared to other NRTIs such as tenofovir-disoproxil-fumarate (TDF), abacavir (ABC), and zidovudine (ZDV) [46,47,51].

### 2.4. Guideline recommendations and special management considerations

Guidelines generally recommend obtaining a weight at each visit, at time of diagnosis, and prior to starting ART, with management for overweight and obesity extrapolated from that of the general population (Table 1). Among the general population, weight loss efforts typically

**Table 1**
Major guideline recommendations for obesity and weight management among PLWH.

| Major Guideline | Baseline Tests | Recommendations |
|---|---|---|
| IDSA Guidelines on Primary Care of Persons with HIV [63] | -Obtain weight at HIV diagnosis | -Weight measurement at every visit<br>-No specific weight/weight loss goal mentioned |
| 2013 ACC/AHA Multisociety Guideline for Management of Overweight and Obesity in Adults [64] | -No specific recommendations | -Does not make distinct recommendations regarding screening or treatment recommendations for PLWH<br>-Goal body mass index <25 kg/m$^2$ or a weight loss of 5–10% of baseline weight within 6 months for those with body mass index ≥25 kg/m$^2$ |
| European AIDS Clinical Society (EACS) 2023 Guidelines [65] | -Obtain body mass index at HIV diagnosis and prior to ART initiation | -Weight management should focus on individualized goals, nutrition, physical activity, intensive evidence-based structured weight management programs, and consideration of metabolic surgery or weight loss medications (i.e., semaglutide, tirzepatide)<br>-Individualized weight goals |

focus on lifestyle modification and if needed pharmacotherapy. Current medications approved for obesity management include orlistat, bupropion-naltrexone, phentermine-topiramate, glucagon-like peptide 1 receptor agonists (GLP1-RA) (i.e., semaglutide, liraglutide), and tirzepatide (GLP1-RA and glucose dependent insulinotropic polypeptide receptor agonists (GIP-RA)). However, scant literature examining the efficacy and safety of these medications among PLWH exists. Published case reports examining orlistat noted temporal recrudescence of HIV viremia in the setting of lipophilic ART raising safety concern among PLWH [58,59]. Several cohort studies have documented effectiveness of GLP1-RA and GIP-RA among PLWH. For semaglutide, a recently published observational study using data from the Centers for AIDS Research Network of Integrated Clinical Systems (CNICS) cohort found an average weight loss of 6.47 kg at 1 year (95% CI -7.67 to -5.18) in patients with HIV [60]. Another retrospective cohort study among PLWH found an average weight loss of 5.4 kg after an average of 13 months of semaglutide [61]. Further, the same study found an association between tirzepatide, a glucose-dependent insulinoptropic polypeptide with GLP-1 and GIP activation, and >5% weight loss in multivariable analysis [61]. In general, with the exception of ART that require low gastric pH for absorption (i.e. atazanavir, rilpivirine), GLP1-RA and GIP-RA are metabolized by endopeptidases and do not have major drug-drug interactions with most ART, making them very reasonable agents for obesity management in this population [62].

## 3. Hypertension

### 3.1. Pathogenesis

The pathogenesis of hypertension among PLWH is incompletely understood and likely multifactorial, including traditional hypertension risk factors such as sociodemographic, hereditary, and behavioral influences as well as HIV-related factors. Proposed mechanisms for HIV and ART-related hypertension include chronic inflammation, immune reconstitution, lipodystrophy, and gut microbial translocation, which have all been linked directly or indirectly to activation of the sympathetic and renin-angiotensin-aldosterone systems, ultimately promoting hypertension [66–70].

### 3.2. Epidemiology

Cohort studies of PLWH have documented widely varied hypertension prevalence, ranging from 4–57% [71–76]. A 2017 meta-analysis of 49 studies (2011–2016) with 63,554 PLWH found an estimated hypertension prevalence of 25.2% (95% CI 21.2%-29.6%), with ART-experienced having higher prevalent hypertension compared to ART-naïve (34.7% versus 12.7%) [77]. A more recent 2021 meta-analysis of 59 studies with 11,101,581 individuals (both PLWH and HIV-negative individuals) found a lower risk of hypertension among PLWH compared to HIV-negative individuals (RR 0.90, 95% CI 0.85–0.96); however, there was significant heterogeneity between included studies ($I^2$ = 97%, p<0.0001) [78]. Interestingly, this study found the relationship varied by geographic location, with higher risk among PLWH in North America (RR 1.12, 95% CI 1.02–1.23) and lower risk among PLWH in Africa (RR 0.75, 95% CI 0.68–0.83) and Asia (RR 0.77, 95% CI 0.63–0.95) [78]. Accurate and precise prevalence estimates of hypertension are challenging due to a plethora of reasons. For example, differences in methodology of data collection, the re-defining of hypertension in 2017 by the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines, and innate demographic differences and varying levels of HIV/AIDS control studied all make it difficult to disentangle the HIV effect on blood pressure.

### 3.3. Factors associated with increased risk of hypertension

Factors associated with increased risk of hypertension among PLWH are similar to the general population, include increasing age [76,77,79–81], elevated body mass index and abdominal obesity [71,72,75,76,80–83], alcohol consumption [71,79], family history [71,79], lack of physical exercise [71], and comorbid medical conditions such as diabetes and hyperlipidemia [75,76,80,81]. HIV-specific factors include longer duration of ART [71,79], longer duration of HIV [75,79,81], lower baseline CD4 count [71], and receipt of ART [74,77]. Rarely have single cohort studies found no association or even a negative association between receiving ART and hypertension [75,84].

### 3.4. Guideline recommendations and special management considerations

The IDSA Guidelines on Primary Care of Persons with HIV and the European AIDS Clinical Society (EACS) 2023 Guidelines recommend obtaining blood pressure (BP) measurements at HIV diagnosis, prior to ART initiation, and screening at subsequent visits whereas the 2017 ACC/AHA Multisociety High Blood Pressure (ACC/AHA) Guidelines and the 2023 European Society of Hypertension (ESH) Guidelines do not provide specific recommendations for PLWH (Table 2). Similarly, guidelines do not make distinct blood pressure goals or management recommendations for PLWH and thus management can follow that of the general population. Regarding goal BP, ACC/AHA, ESH, and EACS guidelines generally recommend a goal BP<130/80 mmHg, particularly for adults with high ASCVD risk, though ESH provides additional age-based treatment targets [65,85,86]. Further, management strategies include lifestyle interventions such as weight loss, dietary reduction of sodium, physical activity, and reduction in alcohol consumption and pharmacotherapy with angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, dihydropyridine calcium channel blockers, and thiazide-type diuretics generally as first-line agents, though providers should check for drug-drug interactions with ART regimen (see Section 7 for recommendations).

## 4. Insulin resistance/type 2 diabetes

### 4.1. Pathogenesis

Data surrounding the association between HIV and type 2 diabetes

**Table 2**
Major guideline recommendations for hypertension among PLWH.

| Major Guideline | Baseline Tests | Recommendations |
|---|---|---|
| IDSA Guidelines on Primary Care of Persons with HIV [63] | -Obtain blood pressure at HIV diagnosis | -Blood pressure screening at every visit<br>-No specific blood pressure goal mentioned |
| European AIDS Clinical Society (EACS) 2023 Guidelines [65] | -Obtain blood pressure at HIV diagnosis and prior to ART initiation | -Blood pressure screening annually<br>-Recommended management follows the European Society of Cardiology and European Society of Hypertension guidelines<br>-Goal BP of <130/80 mmHg |
| 2017 ACC/AHA Multisociety High Blood Pressure Guidelines [86] | -No specific recommendations | -Does not make distinct recommendations regarding screening or treatment recommendations for PLWH<br>-Goal BP of <130/80 mmHg |
| 2023 European Society of Hypertension Guidelines [85] | -No specific recommendations | -Does not make distinct recommendations regarding screening or treatment recommendations for PLWH<br>-Goal BP varies by age, <130/80 mmHg for adults <65 years of age |

(T2DM) is mixed, with positive relationships linked to HIV and ART-associated lipodystrophy, inflammation, pancreatic cell dysfunction, and enhanced gluconeogenesis secondary to heightened glucocorticoid sensitivity [87,88].

### 4.2. Epidemiology

Among the first studies evaluating this association, the Women's Interagency HIV Study, a prospective cohort study (1994–1998) of 1785 women with no prior history of T2DM, found an incidence of T2DM among protease inhibitors (PIs) of 2.8 cases per 100 person-years (2.8%) compared to 1.2% among both reverse transcriptase inhibitors and women on no ART (p=0.01) and 1.4% among women without HIV (p=0.06) [89]. A follow-up study from the Women's Interagency HIV Study found the incidence of T2DM varied based on diagnostic criteria. Specifically, among 1501 women living with HIV, the incidence per 100 person-years was 1.55 (using fasting blood glucose with confirmatory fasting blood glucose) compared to 500 women without HIV (incidence 0.85 per 100 person-years), a finding that reached statistical significance but did not hold when using alternative definitions for T2DM (such as HbA1c, reported T2DM diagnosis, or presence of T2DM medication [90,91]. Shortly thereafter, the Multicenter AIDS Cohort Study (1999–2003) found a 14% prevalence of T2DM among men living with HIV compared to 5% for men without HIV, and an adjusted incident rate per 100 person-years of 4.7 compared to 1.4, respectively (rate ratio = 4.11, 95% CI 1.85–9.16) [92]. In the Swiss HIV Cohort Study, the incidence of T2DM among PLWH was 4.4 per 1000 person-years of follow-up (95% CI 3.7–5.3) but did not have a control comparator [93]. The Data Collection on Adverse Events of Anti-HIV Drugs (D:A:D) cohort found a slightly higher incidence rate of 5.72 per 1000 person-years of follow-up (95% CI 5.31–6.13) but also did not have a control comparator [94]. Using nationally representative survey data 2009–2010 from the Medical Monitoring Project (8610 PLWH) and the National Health and Nutrition Examination Survey (5604 individuals without HIV), a T2DM prevalence of 10.3% (95% CI 9.2%-11.5%) was found. This prevalence was 3.8% higher than adults without HIV (CI 1.8%-5.8%) [95]. Among PLWH in Sub-Saharan Africa, estimates of T2DM also varied greatly, ranging from 1% to 26% in 15 identified studies [96]. While these studies suggest a positive relationship or trend to, others less commonly have found negative relationships between HIV and T2DM.

For example, the Veterans Aging Cohort Study (1999–2011) found an increased incidence rate of T2DM among individuals without HIV compared to PLWH (27 versus 13 per 1000 person-years, p <0.001) [97]. Similarly, using data from the South Carolina Medicaid system and the enhanced HIV/AIDS Reporting System surveillance database (1994–2011), PLWH had lower risk of incident T2DM compared with matched, uninfected individuals (11.4 versus 13.6 per 1000 person-years, p = 0.011) [98]. Important to note, the previously described studies often differed in how T2DM was identified and defined.

### 4.3. Factors associated with increased risk of T2DM

Several risk factors are associated with T2DM among PLWH including advancing age [89,95,97–99], longer duration of HIV infection [95], obesity [89,95,97–99], smoking [97], female gender [98], and non-white race/ethnicity [97,98]. Additionally, medications are strongly implicated in the relationship between T2DM and HIV. Studies using multivariate models to identify factors associated with T2DM have identified cumulative exposure to ART [94,98], PIs [89,93,98,99], and NRTIs [93]. Specific medications implicated have included stavudine, zidovudine, didanosine, indinavir, and dolutegravir [94,99,100]. A meta-analysis of 20,178 individuals and 41 observational studies found increased mean fasting plasma glucose concentrations (pooled mean difference 4.66, 95% CI 2.52–6.80) and increased odds of diabetes among ART-exposed PLWH compared to ART-naïve PLWH (pooled odds ratios 3.85, 95% CI 2.93–5.07) [101]. However, the association of ART with diabetes has not always been consistent. Interestingly, there is some data to suggest newer generation PIs and NRTIs are associated with a lower risk of diabetes [102].

### 4.4. Guideline recommendations and special management considerations

The IDSA Guidelines on Primary Care of Persons with HIV recommends obtaining a random or fasting blood glucose and hemoglobin A1c prior to starting ART; however, after initiation of ART, only plasma glucose criteria should be used for screening and diagnosis of diabetes due to reported effects of ART on HbA1c levels, specifically PIs, NRTIs, and NNRTIs [63,103–105] (Table 3). More specifically, studies have found that HbA1c underestimates the prevalence of type 2 diabetes compared to fasting blood glucose levels due to factors such as increased RBC turnover, low-grade hemolysis, and ART-induced macrocytosis, and a lower HbA1c level of 5.8% improves sensitivity of diagnosing T2DM among PLWH [103,104,106,107]. The ADA agrees with this recommendation to use plasma blood glucose in the diagnosis of diabetes for PLWH and that screening should be performed before starting ART, at time of switching ART, and 3–6 months thereafter [108]. IDSA recommends that for PLWH meeting diagnostic criteria for diabetes, monitoring should be performed every 6 months with a plasma glucose or HbA1c level [63].

While the European AIDS Clinical Society (EACS) 2023 Guidelines provide similar screening recommendations, it also makes pharmacologic management recommendations. Importantly, it recommends the use of GLP1-RA or SGLT2i based on risk profile, highlighting PLWH with known ASCVD, high-risk for ASCVD, chronic kidney disease, heart failure with reduced ejection fraction, and uncontrolled T2DM as populations that would particularly benefit from one or both of the drug classes [65]. In particular, GLP1-RA have proven to be an excellent tool in mitigating ASCVD risk as well as diabetes and weight control. From the CNICS cohort study previously described, in addition to weight loss, PLWH experienced a 1.07% reduction in HbA1c at 1 year with semaglutide, results similar to those without HIV, a finding that has held in other cohort studies [60,61].

**Table 3**
Major guideline recommendations for insulin resistance and type 2 diabetes among PLWH.

| Major Guideline Recommendations | Baseline Tests | Recommendations |
|---|---|---|
| IDSA Guidelines on Primary Care of Persons with HIV [63] | -Obtain random or fasting blood glucose and HbA1c prior to ART initiation | -Once ART initiated, screen with plasma glucose annually; if abnormal, obtain fasting glucose<br>-Once diabetes diagnosed, monitor at least every 6 months with plasma glucose or HbA1c<br>-Consider testing 1–3 months after starting or switching ART<br>-HbA1c is not used to diagnose diabetes, consider threshold cutoff of 5.8%<br>-Goal HbA1c <7% |
| American Diabetes Association [108] | -Obtain fasting blood glucose prior to ART initiation | -Once ART initiated, use only plasma glucose criteria to screen and diagnose diabetes<br>-If initial screening results are normal, fasting blood glucose should be checked annually<br>-Screen with fasting plasma blood glucose at time of switching ART and 3–6 months thereafter<br>-Goal HbA1c <7% for most, but less stringent goals dependent on risk versus benefit evaluation |
| European AIDS Clinical Society (EACS) 2023 Guidelines [65] | -Obtain blood glucose test at HIV diagnosis and prior to ART initiation; if fasting abnormal, consider oral glucose tolerance test | -Uses same diabetes diagnostic criteria as World Health Organization<br>-Screen annually<br>-Cautions that HbA1c in treated PLWH tends to underestimate type 2 diabetes<br>-Glycemic management: Metformin or combination therapy with efficacy; recognizes spectrum of glucose lowering efficacy of GLP1-receptor agonists, insulin, metformin, SGLT2i, sulfonylureas, TZDs, and DPP-4i<br>-Goal HbA1c 6.5–7% |

## 5. Metabolic-dysfunction associated steatotic liver disease

### 5.1. Pathogenesis

Fatty liver disease has been described in PLWH since the early days of the HIV epidemic. While the term non-alcoholic fatty liver disease, or NAFLD, has fallen out of favor for metabolic dysfunction-associated steatotic liver disease, or MASLD, there is considerable overlap in the two disease entities [109] and will be used interchangeably moving forward. Mechanisms postulated to influence the development of MASLD among PLWH include metabolic factors (i.e., dyslipidemia, hypertension, waist circumference, visceral adiposity, and insulin resistance), immunologic/inflammatory factors [110], genetics [95,111,112], medications (via direct drug toxicity and/or metabolism, hypersensitivity reactions, mitochondrial toxicity, and immune reconstitution inflammatory syndrome (IRIS)) [113,114], influence of the gut microbiome [115,116], and HIV itself [117–121].

### 5.2. Epidemiology

Cohort studies examining the prevalence of MASLD among PLWH have reported the prevalence ranging from 26.6–51.0% depending on the population sampled [122–126]. A meta-analysis by Kalligeros et al. of 8230 PLWH and 43 studies found a prevalence of MASLD to be 33.9% based on imaging studies and 48.8% based on biopsy studies; however, these studies had substantial heterogeneity ($I^2$ = 90.62% and 85.80%, respectively) [127]. In a different meta-analysis by Maurice et al. of 10 studies, the prevalence of MASLD based on imaging was 35% and similarly had substantial heterogeneity ($I^2$ = 85.3%) [128]. With the published variability and heterogeneity in prevalence of MASLD, it is important to note that study populations and methods for identifying steatohepatitis have ranged significantly, with majority relying on non-invasive imaging-based techniques for diagnosis.

### 5.3. Factors associated with increased risk of metabolic dysfunction-associated steatotic liver disease

Risk factors associated with MASLD among PLWH include increasing age [124–127,129], male gender [127,129–131], elevated BMI [124,127,128,131], higher waist circumference [126–128,130–132], hypertension [127,128,131], diabetes [127,128,131], dyslipidemia [127,128,131,132], and elevated AST/ALT measurements [125,128,130,131], similar to the general population. Among HIV-specific factors, some studies have identified longer duration of HIV infection [127] and longer duration of ART [127,130,131] to be associated with increased MASLD risk. Further, concurrent infection with hepatitis B or C virus (HBV/HCV) has been shown to alter the risk of MASLD progression to fibrosis [133,134]. Other studies, however, failed to identify increased independent risk with HIV duration [128,132], ART duration [125,128], and HIV viral load [132], though these latter studies frequently adjusted for dyslipidemia or waist circumference, adverse effects commonly associated with both HIV and ART.

Studies that looked at medications specifically had variable effects. From a mechanistic perspective, all antiretroviral drugs have some risk of hepatotoxicity. The most implicated pathogenesis among the different drug classes includes direct drug toxicity or drug metabolism (PIs, NNRTIs), hypersensitivity reactions (NNRTIs), mitochondrial toxicity via inhibition of mitochondrial polymerase gamma (NRTIs), or HBV reactivation (NRTIs) [95,135]. Clinical studies have found cumulative exposure to NRTIs such as stavudine and didanosine as well as PIs to be associated with increased MASLD risk [136–138]. Similarly, among a cross-sectional analysis of the Swiss HIV Cohort Study, current use of TAF was associated with liver steatosis whereas INSTIs were not [124]. On the contrary, in a meta-analysis by Kalligeros et al., the use of NNRTIs, NRTIs, and PIs were not associated with increased MASLD risk. Part of the conflicting evidence may be related to the generation of ART studied and comorbid conditions corrected for in multivariable analysis. For example, first-generation NNRTIs such as efavirenz and nevirapine are more strongly linked to liver toxicity than second-generation NNRTIs such as etravirine, rilpivirine, and doravirine [139].

### 5.4. Guideline recommendations and special management considerations

Major guideline recommendations are summarized in Table 4. The American Association for the Study of Liver Disease (AASLD) does not currently recommend MASLD screening in the general population nor do the guidelines recognize PLWH as a high-risk group for MASLD [109]. Similarly, the IDSA Guidelines on Primary Care of Persons with HIV does not specifically comment on the risk of or screening for MASLD among HIV, but rather focuses on overall liver assessment (i.e., liver enzymes, viral hepatitis serologies) [63]. Contrary to the major American Guidelines, the European AIDS Clinical Society (EACS) recommends periodic MASLD risk assessment for those with HIV and at least one additional risk factor (Table 4) [65].

**Table 4**
Major guideline recommendations for MASLD among PLWH.

| Major Guideline | Baseline Tests | Recommendations |
|---|---|---|
| IDSA Guidelines on Primary Care of Persons with HIV [63] | -Assess for evidence of liver damage, hepatitis, or systemic infection with liver enzymes and viral hepatitis serologies at HIV diagnosis | -Does not make distinct recommendations regarding MASLD screening or treatment recommendations for PLWH |
| American Association for the Study of Liver Disease (AASLD) [109] | -No specific recommendations | -Does not recommend MASLD screening in general population or PLWH<br>-Does not specifically recognize PLWH as high-risk group for MASLD |
| European AIDS Clinical Society (EACS) [65] | -Perform liver disease risk assessment and liver enzymes at HIV diagnosis and prior to ART initiation | -Repeat risk assessment annually<br>-Repeat liver enzymes 3–12 months, more frequent if treatment with hepatotoxic drugs<br>-Recommends FIB-4 or NAFLD fibrosis score risk assessment for PLWH at risk of NAFLD (at least one of following factors: NAFLD suggested by ultrasound, overweight, metabolic syndrome, persistent elevation of ALT, exposure to d-drugs) |

Regarding potential treatment for MASLD, there are currently no FDA-approved medications for the treatment of MASLD at any disease stage for the general population. However, clinical trials have shown drugs approved for associated comorbidities, such as thiazolidinediones (i.e., pioglitazone), GLP-1 receptor agonists (i.e., liraglutide, semaglutide), vitamin E, tirzepatide, lipophilic statins, caffeine, and SGLT2 inhibitors to also have benefit in MASLD [140,141]. This benefit is likely derived by their ability to improve insulin sensitivity, weight loss, and hepatic steatosis.

These medications are likely to have similar effects among PLWH. A randomized controlled trial among HIV-positive individuals with prediabetes who had evidence by fatty liver on ultrasound or controlled attenuation parameter (CAP) were randomized to pioglitazone or placebo. At 48 weeks, pioglitazone reduced CAP, liver stiffness, and fasting plasma glucose compared to control [142]. Another randomized, double-blinded multicenter trial among 61 PLWH found tesamorelin, a synthetic peptide analogue of growth hormone-releasing hormone, to significantly reduce central adiposity and hepatic fat fraction compared to placebo [140,143]. There are several novel medications currently in clinical trials aimed at targeting development of hepatic steatosis, oxidative stress, inflammation, and fibrosis [144,145].

## 6. Dyslipidemia

### 6.1. Pathogenesis

Several mechanistic pathways have been elucidated for dyslipidemia among PLWH. HIV is associated with higher levels of proatherogenic particles such as low-density lipoprotein cholesterol (LDL-C), particularly small, dense oxidized LDL-C, very low-density lipoprotein cholesterol (VLDL-C), and triglycerides (TG) and lower levels and functionality of anti-atherogenic particles such as high-density lipoprotein (HDL-C) [146,147]. Additionally, HIV-induced immune activation results in endothelial and smooth muscle cell dysfunction, infiltration of activated monocytes and macrophages in the endothelium, and foam cell formation [15,148,149]. All these factors contribute to enhanced atherogenesis and a noncalcified plaque phenotype prone to rupture [148].

### 6.2. Epidemiology

Similar to the general population, dyslipidemia remains an important and prevalent atherosclerotic disease risk factor. In a meta-analysis of 39 peer-reviewed publications of 13,698 PLWH, dyslipidemia had a 39.5% prevalence [150]. In African and Asian-based retrospective cohort studies specifically, reported estimated prevalence of dyslipidemia among PLWH were even higher at 55.2–86.6% and 82%, respectively [62,151–153]. This prevalence of dyslipidemia is expected to continue to increase over time. Using the PEARL Model (ProjEcting Age, multimoRbidity, and polypharmacy), a forecasted simulation model of PLWH using ART, the prevalence of dyslipidemia in the United States is projected to rise from 42% in 2020 to 48% in 2030 [154].

### 6.3. Factors associated with increased risk of dyslipidemia

Factors associated with dyslipidemia among PLWH are similar to that of the general population, including age [62,151,155,156], smoking [157], alcohol intake [152,157], and comorbid conditions such as overweight/obesity and central adiposity [84,151,155,156,158,159], hyperglycemia and diabetes [155,159], and hypertension [159].

Generally, the presence of HIV, the use of ART, and longer ART duration are associated with higher triglycerides, total cholesterol, and LDL-C and lower HDL-C [84,159–163]. Analyses have also found conflicting results regarding the risk of dyslipidemia with varying levels of disease control [151,155,159]; however, this relationship direction likely depends on cholesterol subtype. Lower CD4 is associated with increased risk of higher triglycerides and lower HDL but decreased risk of higher total cholesterol and LDL-C [156,158,163,164].

Several studies have looked at the effect of specific ART on dyslipidemia. A 2021 cohort study examining the incidence of dyslipidemia among PLWH receiving different ART found participants receiving INSTIs had lower incidence rate of dyslipidemia compared to those receiving PIs (adjusted incidence rate ratio 0.71; CI 0.59–0.85) but higher incidence rate compared to those receiving NNRTIs (adjusted incidence rate ratio 1.35; CI 1.15–1.58) [165]. Multiple other cohort studies have corroborated the increased risk of PI-associated dyslipidemia compared to INSTIs [166–168]. A 2023 systematic review of 73 studies examining the impact of contemporary ART on dyslipidemia further confirmed this finding, again demonstrating the highest incidence of dyslipidemia in PIs followed by INSTIs and then NNRTIs [169]. Within the drug classes, older generation PIs (i.e., indinavir, ritonavir, nelfinavir, etc.) have more adverse effects on dyslipidemia than do newer PIs (i.e., atazanavir, darunavir) [170]. Among INSTIs, EVG/c and RAL have been shown to have greater risk of dyslipidemia than DTG [165]. NNRTIs generally have fewer adverse effects on lipids and among NRTIs, thymidine analogs (i.e., zidovudine, didanosine, lamivudine, stavudine, etc.) have greater risk of dyslipidemia compared to non-thymidine analogs (i.e., abacavir, tenofovir) [170]. The newer formulation of TAF, like its increased risk of weight gain, has worse lipid effects compared to the older formulation tenofovir disoproxil fumarate [170].

### 6.4. Guideline recommendations and special management considerations

Major guideline recommendations are summarized in Table 5 and generally recommend obtaining a lipid profile at HIV diagnosis, prior to ART initiation, and after starting or switching ART. However, the guidelines differ in their recommended risk stratification tools (i.e. ACC/AHA Pooled Cohort Equation, Framingham Risk Score, SCORE2/SCORE2-OP, etc.) and how frequently to repeat the lipid profiles based on the starting lipid profile and risk assessments. Goal LDL-C levels are extrapolated from the risk-stratified goals of the general population; however, the 2018 AHA/ACC Multisociety Guideline on the Management of Blood Cholesterol (2018 AHA/ACC Cholesterol), the National Lipid Association (NLA), and the United States Department of

**Table 5**
Major guideline recommendations for dyslipidemia among PLWH.

| Major Guideline | Baseline Tests | Recommendations |
|---|---|---|
| IDSA Guidelines on Primary Care of Persons with HIV [63] | -Obtain lipid profile prior to ART initiation | -Repeat every 5 years if normal<br>-Repeat every 6–12 months if abnormal or other CV risk factors<br>-If abnormal, repeat fasting<br>-Consider testing 1–3 months after starting or switching ART<br>-Goal and management per NLA Part 2 and 2018 AHA/ACC Guidelines |
| United States Department of Health and Human Services (DHHS) Guidelines [172] | -Obtain lipid profile at HIV diagnosis; if random levels abnormal, fasting lipids should be obtained | -Repeat lipid profile 1–3 months after ART initiation or modification<br>-If normal baseline lipid profile but with ASCVD risk, repeat lipid profile at 12 months<br>-If normal baseline lipid profile and without ASCVD risk, repeat lipid profile every 5 years or if clinically indicated<br>-Initiate high-intensity statin therapy for adults 40–75 years of age with ≥20% 10-year ASCVD risk, known ASCVD, or LDL-C ≥190 mg/dL<br>-Initiate at least moderate-intensity therapy for adults 40–75 years of age with T2DM, ASCVD risk 5% to <20%, and consider if ASCVD risk is <5%<br>-Moderate-intensity statin therapy includes atorvastatin 20 mg daily, rosuvastatin 10 mg daily, or pitavastatin 4 mg daily |
| European AIDS Clinical Society (EACS) 2023 Guidelines [65] | -Obtain lipid profile at HIV diagnosis and prior to ART initiation | -Repeat yearly if high/very high risk, 3–5 years if low/moderate risk (based on SCORE2 and SCORE2-OP)<br>-Drug treatment if established CVD or DM or 10-year CVD risk ≥10%<br>-LDL-C reduction goal dependent on risk estimation by SCORE2 and SCORE2-OP; for high risk and very high risk, goal LDL-C is ≥50% reduction from baseline and LDL-C<70 mg/dL and LDL-C<55 mg/dL, respectively |
| 2018 AHA/ACC/ Multisociety Guideline on the Management of Blood Cholesterol [1] | -Obtain fasting lipid profile and perform assessment of ASCVD risk factors prior to ART initiation | -HIV recognized as an ASCVD risk enhancer<br>-Pooled cohort equations may underestimate ASCVD risk in HIV<br>-Repeat fasting lipid profile and risk assessment 4–12 weeks after starting ART, CAC scan can improvement risk assessment<br>-Lifestyle improvements, smoking cessation<br>-In adults 40–75 years of age with LDL-C 70–189 mg/dL who have a 10-year ASCVD risk of ≥7.5%, consider moderate or high-intensity statin, if ≥5% consider moderate-intensity statin<br>-In adults 40–75 years of age with T2DM, start at least a moderate-intensity statin in primary prevention<br>-Goal LDL-C is dependent on risk evaluation and presence of known ASCVD; goal LDL-C ranges from ≥30–50% reduction from baseline and <70 mg/dL or <100 mg/dL |
| National Lipid Association Part 2 [171] | -Obtain fasting lipid profile prior to ART initiation | -Repeat after starting ART<br>-HIV recognized as additional ASCVD risk factor for risk stratification<br>-Risk stratify based on NLA Part 1 with HIV as additional risk factor, use ATP III Framingham Risk Score or ACC/AHA PCE<br>-Goal non-HDL-C and LCL-C as described in NLA Part 1<br>-Lifestyle interventions, smoking cessation, nutritional counseling, weight management<br>-Statin therapy is first-line for elevated LDL-C and non-HDL-C; NLA Expert Panel recommends atorvastatin, rosuvastatin, pitavastatin as preferred agents<br>-Goal LDL-C is dependent on risk evaluation; goal LDL-C levels include <70 mg/dL and <100 mg/dL depending on evaluation |

Health and Human Services (DHHS) Panel importantly recognize HIV as a specific ASCVD risk enhancer that must be factored into the overall risk assessment [1,171,172]. Further, the 2018 AHA/ACC Cholesterol Guidelines and the DHHS Panel state that risk-enhancing features such as HIV may favor statin therapy in patients with borderline 10-year risk.

Some guidelines make specific recommendations regarding cholesterol-lowering agents for PLWH. The National Lipid Association Guideline recommends pitavastatin as a first-line lipid-lowering treatment in PLWH because of no drug-drug interactions with ART [171]. The EACS 2023 Guidelines provide advice on lipid lowering therapy dosing and expected interactions for a wide range of cholesterol-lowering therapy, including statins, bempedoic acid, ezetimibe, PCSK9i, and icosapent ethyl [65]. The DHHS Panel, which is endorsed by the ACC, AHA, and HIV Medicine Association (HIVMA), recommends pitavastatin 4 mg daily, atorvastatin 20 mg daily, or rosuvastatin 10 mg daily for moderate statin intensity therapy [172].

Unlike many of the other cardiometabolic recommendations, newer guideline recommendations surrounding dyslipidemia (i.e. DHHS) are informed by a randomized controlled trial. The REPRIEVE Trial is the largest randomized trial to-date among PLWH that evaluated the effect of pitavastatin on cardiovascular clinical endpoints [173]. REPRIEVE found that among 7769 PLWH, individuals who received pitavastin had a lower risk of major cardiovascular events than those who received placebo over a median follow-up of 5.1 years. A mechanistic substudy of REPRIEVE demonstrated that among PLWH at low to moderate ASCVD risk, 24 months of pitavastatin reduced noncalcified plaque volume and progression, lipid oxidation, and arterial inflammation [31]. The Effect of PCSK9 Inhibition on Cardiovascular Risk in Treated HIV Infection is an ongoing clinical trial investigating the impact of alirocumab on cholesterol, inflammatory markers, and non-calcified plaque in individuals with HIV (NCT 03207945).

While these guidelines provide helpful starting points for statin therapy among PLWH, drug-drug interactions (DDIs) with ART and statins are well-studied beyond these recommendations. Protease inhibitors, pharmacokinetic boosters (i.e., atazanavir, cobicistat, etc.), and non-nucleoside reverse transcriptase inhibitors interact with CYP450 enzymes, creating DDIs with statins. Alternatively, no expected significant DDIs exist with nucleoside reverse transcriptase inhibitors, integrase strand inhibitors, chemokine receptor-5 inhibitors, and fusion inhibitors [65,172,174–176]. As such, providers should tailor statin doses to specific ART regimens. For example, first-line ART today consists of a backbone of two nucleoside reverse transcriptase inhibitors in combination with a third ART drug (either integrase strand inhibitors, non-nucleoside reverse transcriptase inhibitors, or protease inhibitors). If providers use the recommended first-line combination of two nucleoside reverse transcriptase inhibitors with an integrase strand inhibitor, no statin dose adjustment is needed [172]. If an additional cholesterol-lowering medication is required, non-statin therapies do not appear to have DDIs with ART though these medications – adenosine triphosphate citrate lyase inhibitors (i.e., bempedoic acid), intestinal cholesterol absorption inhibitors (i.e., ezetimibe), PCSK9i (i.e., evolocumab, alirocumab), fibrates, and fish oil/omega-3 (i.e. icosapent ethyl) – are less studied to date [65,172,174–176].

## 7. An evidence-based, simplified approach to cardiometabolic diseases in PLWH

Similar to most major guidelines, we view HIV as a well-proven cardiovascular disease risk factor. HIV is associated with increased risk of atherosclerotic disease, myocardial infarction, stroke, heart failure, and sudden cardiac death [2–11]. Through this review, we also add HIV as a well-proven cardiometabolic disease risk factor. We recommend performing an overall cardiovascular risk assessment in PLWH at least annually and addressing modifiable risk factors at each follow-up visit. Risk calculators include standard ASCVD risk assessment models such as the 2008 Framingham Heart Study risk algorithm [177] and 2013 American College of Cardiology/American Heart Association Pooled Cohort Equations (PCEs) [178] and HIV-specific risk assessment models that incorporate HIV and ART-specific variables such as the Data Collection on Adverse Events of Anti-HIV Drugs (D:A:D) model [156] and the Veterans Aging Cohort Study index scores [179,180], all of which have comparable risk prediction performance among PLWH [181]. However, even these models tend to underestimate true risk among PLWH [181–184]. This risk underestimation is likely derived from the presence of additional risk enhancers that make some PLWH at increased risk than predicted, including lower CD4 count and higher HIV viremia [3,5,30,184–186] as well as coinfections such as hepatitis C [187,188]. Not to mention, the role of inequities in social determinants of health that PLWH are often faced with, including disparities in care access, stigmatization, social support, neurocognitive decline, and substance use contribute to increased ASCVD risk [22–29]. We recommend the current ACC/AHA guideline-based approach for primary prevention of PLWH starting with an assessment of their 2013 PCE ASCVD risk while also understanding its limitations/underestimations. For example, in a recent retrospective study comparing coronary artery plaque burden between asymptomatic PLWH and people without HIV, of those with similar calculated ASCVD risk, PLWH had more coronary plaque than their non-HIV comparison [189]. We also recommend consideration of the PREVENT risk score when necessary to refine risk assessment based on social determinants of health and concerns for kidney disease. All PLWH should be assessed for other risk enhancers that may drive their risk higher, and strong consideration should be made for coronary artery calcium assessment.

Fig. 1 and Table 6 highlight our recommendations for cardiometabolic disease screening, monitoring, pharmacologic management, and multidisciplinary care. At a minimum, providers should perform baseline weight, blood pressure, fasting blood glucose, liver enzymes, viral hepatitis serologies, and lipid profile measurements at the time of HIV diagnosis and periodically thereafter. If suspicion for MASLD arises, start by calculating a FIB-4 or NAFLD Fibrosis Score followed by consideration of liver ultrasound or Fibroscan. Any change in ART regimen warrants repeat evaluation 1–3 months thereafter. For patients who have not yet achieved their weight, blood pressure,

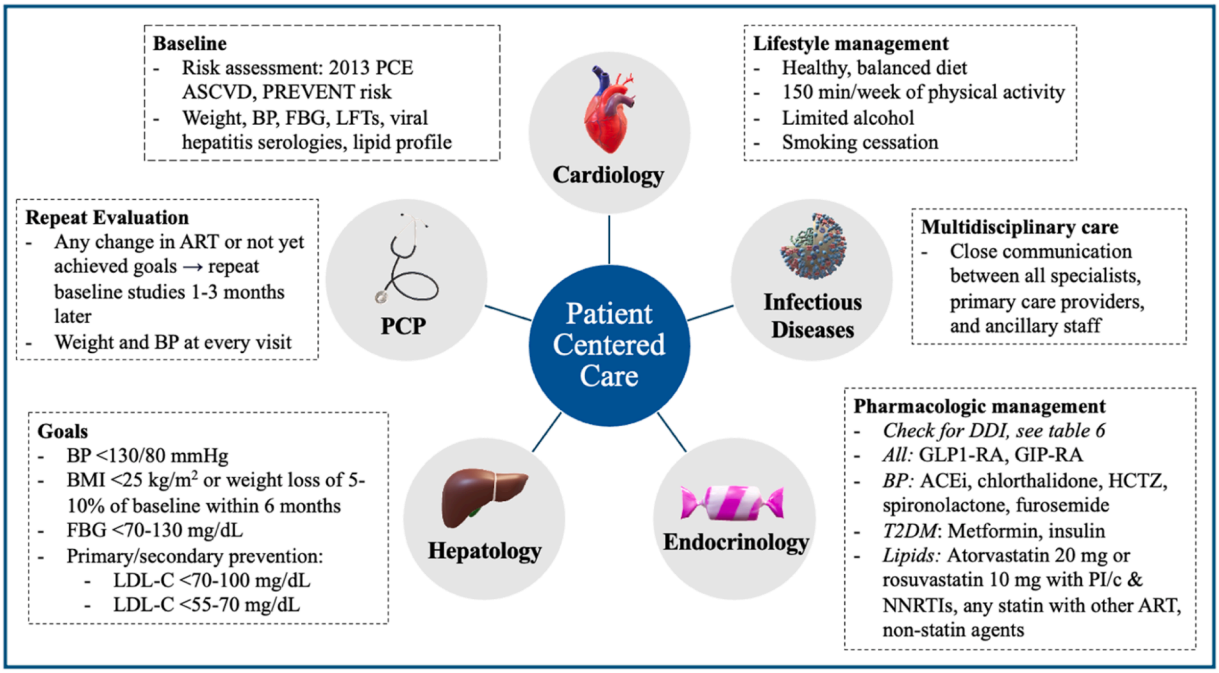



**Fig. 1.** Schema of recommended multidisciplinary cardiometabolic care for PLWH. Abbreviations: PCE, pooled cohort equation; ASCVD, atherosclerotic cardiovascular disease; BP, blood pressure; FBG, fasting blood glucose; LFTs, liver function tests; ART, antiretroviral therapy; BMI, body mass index; DDI, drug-drug interactions; ACEi, angiotensin-converting enzyme inhibitor; HCTZ, hydrochlorothiazide; PI/c, protease inhibitors/cobicistat; NNRTIs, non-nucleoside reverse transcriptase inhibitors.

**Table 6**
Quick reference for cardiometabolic diseases management among PLWH.

| *Cardiometabolic disease* | *Baseline tests* | *Screening/ Monitoring* | *Pharmacologic management* |
|---|---|---|---|
| **Obesity** | -Obtain weight at time of diagnosis and/or prior to ART initiation | -Repeat weight measurement at frequency of follow-up visits | -Avoid orlistat<br>-GLP1-RA and GIP-RA are effective and safe, but caution with ART that require low gastric pH for absorption |
| **Hypertension** | -Obtain blood pressure at time of diagnosis and/or prior to ART initiation | -Repeat blood pressure measurement at frequency of follow-up visits | -Use ACE inhibitors (caution with fosinopril), chlorthalidone, hydrochlorothiazide, spironolactone, and furosemide at usual dose with any ART<br>-Caution/close monitoring with specific ARBs (valsartan, irbesartan, losartan), beta blockers, calcium channel blockers, eplerenone, and torsemide combined with PIs and specific NNRTIs (EFV/ETR/ NVP) due to DDI<br>-In general, NRTIs, integrase inhibitors (unless combined with cobicistat), and fusion inhibitors have minimal DDI with anti-hypertensive agents |
| **Insulin resistance/ T2DM** | -Obtain random or fasting blood glucose at time of HIV diagnosis | -HbA1c in HIV tends to underestimate T2DM<br>-Screen with random plasma glucose at least annually; if abnormal, check FBG<br>-If switching ART, screen with FBG at time of switch and 3 months later<br>-If T2DM diagnosed, monitor with FBG every 6 months | -Use metformin (close monitoring with DTG and BIC, increase metformin AUC), GLP-1 and GIP agonists (caution with ART that require low gastric pH for absorption), thiazolidinediones, and insulin<br>-Caution/closing monitoring with 1) sulfonylureas and PIs, NNRTIs, and EVG/c (variables effects on glipizide, glimepiride, and glyburide); 2) DPP-4i and PIs, EFV/ETR/ NVP, and EVG/c (variable effects on saxagliptin AUC); and 3) SGLT2i and PI/r (decreases canagliflozin AUC) |
| **Metabolic-dysfunction associated steatotic liver disease** | -Obtain liver enzymes and viral hepatitis serologies at time of diagnosis | -Repeat liver enzymes periodically if treatment includes hepatotoxic drugs | -Similar to general population, pharmacologic therapy for MASLD is still under investigation |
| **Dyslipidemia** | -Obtain lipid profile at time of diagnosis and/or prior to ART initiation | -Repeat lipid profile 1–3 months after starting ART<br>-Use an ASCVD risk calculator to determine frequency thereafter | -For statins, use atorvastatin 20 mg, rosuvastatin 10 mg, pitavastatin 4 mg, or fluvastatin 80 mg while titrating carefully and monitoring for side effects with any ART<br>-No expected DDIs with adenosine triphosphate citrate lyase inhibitors (i.e., bempedoic acid), intestinal cholesterol absorption inhibitors (i.e., ezetimibe), PCSK9is (i.e., evolocumab, alirocumab), fibrates, and fish oil/omega-3 (i.e., icosapent ethyl)<br>-No expected significant DDIs with integrase strand inhibitors, nucleoside reverse transcriptase inhibitors, chemokine receptor-5 inhibitors, and fusion inhibitors<br>-Avoid lovastatin and simvastatin with PIs and pharmacokinetic boosters such as cobicistat; avoid bile acid sequestrants |

*ART, antiretroviral therapy; GLP-1, glucagon-like peptide-1; GIP, glucose-dependent insulinotropic polypeptide; ACE, angiotensin-converting enzyme; ARB, angiotensin II receptor blockers; PI, protease inhibitor; NNRTI, non-nucleoside reverse transcriptase inhibitor; EFV, efavirenz; ETR, etravirine; NVP, nevirapine; DDI, drug-drug interaction; NRTI, nucleoside reverse transcriptase inhibitor; T2DM, type 2 diabetes; HbA1c, hemoglobin A1c; FBG, fasting blood glucose; DTG, dolutegravir; BIC, bictegravir; AUC, area under the curve; EVG/c, elvitegravir/cobicistat; DPP-4i, dipeptidyl peptidase-4 inhibitors; SGLT2i, sodium-glucose transport protein 2 inhibitors; PI/r, protease inhibitor/ ritonavir; ASCVD, atherosclerotic cardiovascular disease; PCSK9i, proprotein convertase subtilisin/kexin type 9 inhibitors.

diabetes, or lipid goals, repeat evaluation should occur at the same frequency as the general population, as recommended by major guidelines, until goals are achieved.

Regarding goals for cardiometabolic diseases among PLWH, our recommendations are adopted from the previously summarized guidelines, with trends towards more strict goals. For secondary prevention, we recommend intensive LDL-C lowering, at least under 70 mg/dL if not <55 mg/dL based on level of risk [1]. For primary prevention, a slightly more lenient LDL-C goal of <100 mg/dL is reasonable and varies depending on overall risk assessment. The following goals apply for both primary and secondary ASCVD prevention – for overweight and obesity (BMI ≥25 kg/m$^2$), target a body mass index <25 kg/m$^2$ or a weight loss of 5–10% of baseline weight within 6 months [190]. For blood pressure, we follow the 2017 ACC/AHA Multisociety High Blood Pressure guidelines goal of <130/80 mmHg [86]. For diabetes, we recommend a fasting blood glucose of 70–130 mg/dL as recommended by the ADA for the general population [191]. Finally, for MASLD, treatment goals should focus on prevention by targeting the same cardiometabolic goals just discussed.

At the cornerstone of cardiometabolic disease management, similar to the general population, is therapeutic lifestyle modifications. Counseling on lifestyle measures should include healthy and balanced dietary patterns, 150 min/week of physical activity, limited alcohol consumption, and smoking cessation. Pharmacologic decisions should be based on individual comorbidities. In particular, we would like to highlight SGLT2i and GLP1-RA as they have proven beneficial in a host of cardiometabolic diseases and ASCVD. For example, for a patient with type 2 diabetes and chronic kidney disease or heart failure, we recommend SGLT2i. While canagliflozin requires dose-adjustment and extra monitoring with PIs/ritonavir, most NNRTIs, NRTIs, and integrase inhibitors and SGLT2i do not have significant DDIs [172] (Table 6). Further, for a

patient with type 2 diabetes and obesity, known ASCVD, high-risk for ASCVD, or MASLD, we strongly recommend a GLP1-RA due to its well-established efficacy and lack of significant DDIs with ART. In fact, even in the absence of type 2 diabetes, GLP1-RA are known to improve weight loss, reduce major cardiovascular events in individuals with overweight/obesity and established ASCVD, improve functional status in obese individuals with heart failure with preserved ejection fraction (HFpEF), and improve MASLD [192–194]. We also follow DHHS recommendations for statin therapy, which are directly informed by the REPRIEVE trial [172,173]. For primary prevention among adults 40–75 years of age with T2DM, ASCVD risk 5% to <20%, and possibly if ASCVD risk is <5%, start at least a moderate-intensity statin. For secondary prevention, LDL-C≥190 mg/dL, and ≥20% 10-year ASCVD risk, start a high-intensity statin. When prescribing statin therapy, pay close attention to the ART regimen before dosing (Table 6) [1]. In general, ART regimens that include only NRTIs (typical backbone), INSTIs, chemokine receptor-5 inhibitors, and fusion inhibitors do not need statin adjustments. For all other ART combinations, targeting doses of atorvastatin 20 mg, rosuvastatin 10 mg, pitavastatin 4 mg, or fluvastatin 80 mg with close monitoring are reasonable moderate-intensity doses, with addition of non-statin agents, which are not expected to have significant DDIs with ART, to achieve goal LDL-C.

Given the possibility of DDIs with ART, clinicians should routinely use one of several databases/online tools to check for DDIs. Several examples of tools include the EACS 2023 Guidelines [65], the University of Liverpool Interaction Checker [175], the Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV developed by DHHS [172], the World Health Organization's Table of Drug Interactions with Antiretroviral Drugs [176], and the New York State Department of Health Aids Institute ART Drug-Drug Interactions [174]. Even then, the significance of interactions is challenging to predict. We recommend close monitoring for both therapeutic efficacy and concentration-dependent toxicities. We provide simplified recommendations for pharmacologic management in Table 6 to provide a quick reference for providers. Moreover, given the medications at risk for DDIs are managed by multiple providers – primary care providers, infectious diseases specialists, cardiologists, and ancillary staff – it is important that multidisciplinary teams are in communication to avoid adverse drug effects, optimize risk factors and HIV care, and most importantly keep the patient at the center of the care (Fig. 1).

Important to reiterate, most guideline recommendations for cardiometabolic are derived via casual inference from retrospective cohort studies previously discussed. Randomized clinical trials such as REPRIEVE and SMART serve as the foundation and motivation for future clinical trials within this space [31].

Finally, we close our recommendations with a call to action: in order to improve and optimize cardiovascular and cardiometabolic disease among PLWH, it takes a multifactorial and multidisciplinary approach by primary care physicians, subspecialists, and ancillary providers – we must all work together to reduce disparities in the delivery of evidence-based cardiovascular care, lessen HIV-related stigma and discrimination, increase retention and care coordination, and further our knowledge regarding the unique cardiovascular risks of PLWH through ongoing clinical trials and implementation research.

## 8. Conclusions

PLWH experience a disproportionate burden of cardiometabolic diseases with high rates of obesity, hypertension, insulin resistance, MASLD, and dyslipidemia. This burden is driven by both general ASCVD risk factors as well as HIV and ART-specific factors. While many major guidelines recognize HIV as an ASCVD risk enhancer, there are gaps regarding HIV-specific cardiometabolic disease screening and management. As such, more high-quality, large-scale clinical trials on cardiovascular and cardiometabolic disease prevention and management are needed among PLWH to guide care among this high-risk patient population. For now, we must continue to coordinate our management strategies in a multidisciplinary fashion to optimize patient-centered care.

## Statement of funding

The authors did not have specific financial support for the research, authorship, and/or publication of this article. Declaration of interests are listed elsewhere.

## CRediT authorship contribution statement

**Elizabeth A. Kobe:** Writing – review & editing, Writing – original draft, Visualization, Conceptualization. **Aarti Thakkar:** Writing – review & editing. **Sarina Matai:** Writing – review & editing, Visualization. **Esra Akkaya:** Writing – review & editing. **Neha J. Pagidipati:** Writing – review & editing. **Robert W. McGarrah:** Writing – review & editing. **Gerald S. Bloomfield:** Writing – review & editing. **Nishant P. Shah:** Writing – review & editing, Writing – original draft, Conceptualization.

## Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

Neha J. Pagidipati reports financial support was provided by Amgen. Neha J. Pagidipati reports financial support was provided by AstraZeneca. Neha J. Pagidipati reports financial support was provided by Baseline Study LLC. Neha J. Pagidipati reports financial support was provided by Boehringer Ingelheim. Neha J. Pagidipati reports financial support was provided by Duke University Duke Clinical Research Institute. Neha J. Pagidipati reports financial support was provided by Eggland's Best. Neha J. Pagidipati reports financial support was provided by Eli Lilly and Company. Neha J. Pagidipati reports financial support was provided by Novartis. Neha J. Pagidipati reports financial support was provided by Novo Nordisk Pharmaceuticals. Neha J. Pagidipati reports financial support was provided by Sanofi-S.A. Neha J. Pagidipati reports financial support was provided by Verily Sciences Research Company. Nishant P. Shah reports financial support was provided by Amgen Inc. Nishant P. Shah reports financial support was provided by Janssen. Nishant P. Shah reports financial support was provided by National Institutes of Health. Nishant P. Shah reports a relationship with Esperion Therapeutics Inc that includes: consulting or advisory. Nishant P. Shah reports a relationship with Amgen Inc that includes: consulting or advisory. Nishant P. Shah reports a relationship with Novartis that includes: consulting or advisory. Neha J. Pagidipati reports a relationship with AstraZeneca that includes: consulting or advisory. Neha J. Pagidipati reports a relationship with Boehringer Ingelheim that includes: consulting or advisory. Neha J. Pagidipati reports a relationship with Esperion Therapeutics Inc that includes: consulting or advisory. Neha J. Pagidipati reports a relationship with Eli Lilly and Company that includes: consulting or advisory. Neha J. Pagidipati reports a relationship with Novo Nordisk Pharmaceuticals SA that includes: consulting or advisory. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## References

[1] Grundy SM, Stone NJ, Bailey AL, et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA guideline on the management of blood cholesterol: a report of the American college of cardiology/American heart association task force on clinical practice guidelines. Circulation 2019;139(25):e1082–143. https://doi.org/10.1161/CIR.0000000000000625.

[2] Shah ASV, Stelzle D, Lee KK, et al. Global burden of atherosclerotic cardiovascular disease in people living with HIV: systematic review and meta-analysis. Circulation 2018;138(11):1100–12. https://doi.org/10.1161/CIRCULATIONAHA.117.033369.

[3] Freiberg MS, Chang CC, Kuller LH, et al. HIV infection and the risk of acute myocardial infarction. JAMA Intern Med 2013;173(8):614–22. https://doi.org/10.1001/jamainternmed.2013.3728.

[4] Triant VA, Lee H, Hadigan C, et al. Increased acute myocardial infarction rates and cardiovascular risk factors among patients with human immunodeficiency virus disease. J Clin Endocrinol Metab 2007;92(7):2506–12. https://doi.org/10.1210/jc.2006-2190.

[5] Silverberg MJ, Leyden WA, Xu L, et al. Immunodeficiency and risk of myocardial infarction among HIV-positive individuals with access to care. J Acquir Immune Defic Syndr 2014;65(2):160–6. https://doi.org/10.1097/QAI.0000000000000009.

[6] Paisible AL, Chang CC, So-Armah KA, et al. HIV infection, cardiovascular disease risk factor profile, and risk for acute myocardial infarction. J Acquir Immune Defic Syndr 2015;68(2):209–16. https://doi.org/10.1097/QAI.0000000000000419.

[7] Butt AA, Chang CC, Kuller L, et al. Risk of heart failure with human immunodeficiency virus in the absence of prior diagnosis of coronary heart disease. Arch Intern Med 2011;171(8):737–43. https://doi.org/10.1001/archinternmed.2011.151.

[8] Chow FC, Regan S, Feske S, et al. Comparison of ischemic stroke incidence in HIV-infected and non-HIV-infected patients in a US health care system. J Acquir Immune Defic Syndr 2012;60(4):351–8. https://doi.org/10.1097/QAI.0b013e31825c7f24.

[9] Freiberg MS, Chang CH, Skanderson M, et al. Association between HIV infection and the risk of heart failure with reduced ejection fraction and preserved ejection fraction in the antiretroviral therapy era: results from the veterans aging cohort study. JAMA Cardiol 2017;2(5):536–46. https://doi.org/10.1001/jamacardio.2017.0264.

[10] Sico JJ, Chang CC, So-Armah K, et al. HIV status and the risk of ischemic stroke among men. Neurology 2015;84(19):1933–40. https://doi.org/10.1212/WNL.0000000000001560.

[11] Tseng ZH, Secemsky EA, Dowdy D, et al. Sudden cardiac death in patients with human immunodeficiency virus infection. J Am Coll Cardiol 2012;59(21):1891–6. https://doi.org/10.1016/j.jacc.2012.02.024.

[12] Deeks SG. HIV infection, inflammation, immunosenescence, and aging. Annu Rev Med 2011;62:141–55. https://doi.org/10.1146/annurev-med-042909-093756.

[13] Kaplan RC, Sinclair E, Landay AL, et al. T cell activation predicts carotid artery stiffness among HIV-infected women. Atherosclerosis 2011;217(1):207–13. https://doi.org/10.1016/j.atherosclerosis.2011.03.011.

[14] Bahrami H, Budoff M, Haberlen SA, et al. Inflammatory markers associated with subclinical coronary artery disease: the multicenter AIDS cohort study. J Am Heart Assoc 2016;5(6). https://doi.org/10.1161/JAHA.116.003371.

[15] Burdo TH, Lo J, Abbara S, et al. Soluble CD163, a novel marker of activated macrophages, is elevated and associated with noncalcified coronary plaque in HIV-infected patients. J Infect Dis 2011;204(8):1227–36. https://doi.org/10.1093/infdis/jir520.

[16] Hsu DC, Ma YF, Hur S, et al. Plasma IL-6 levels are independently associated with atherosclerosis and mortality in HIV-infected individuals on suppressive antiretroviral therapy. AIDS 2016;30(13):2065–74. https://doi.org/10.1097/QAD.0000000000001149.

[17] McKibben RA, Margolick JB, Grinspoon S, et al. Elevated levels of monocyte activation markers are associated with subclinical atherosclerosis in men with and those without HIV infection. J Infect Dis 2015;211(8):1219–28. https://doi.org/10.1093/infdis/jiu594.

[18] Ntsekhe M, Baker JV. Cardiovascular disease among persons living with hiv: new insights into pathogenesis and clinical manifestations in a global context. Circulation 2023;147(1):83–100. https://doi.org/10.1161/CIRCULATIONAHA.122.057443.

[19] Hsue PY, Hunt PW, Sinclair E, et al. Increased carotid intima-media thickness in HIV patients is associated with increased cytomegalovirus-specific T-cell responses. AIDS 2006;20(18):2275–83. https://doi.org/10.1097/QAD.0b013e3280108704.

[20] Group DADS, Friis-Moller N, Reiss P, et al. Class of antiretroviral drugs and the risk of myocardial infarction. N Engl J Med 2007;356(17):1723–35. https://doi.org/10.1056/NEJMoa062744.

[21] Group DADS, Sabin CA, Worm SW, et al. Use of nucleoside reverse transcriptase inhibitors and risk of myocardial infarction in HIV-infected patients enrolled in the D:A:D study: a multi-cohort collaboration. Lancet 2008;371(9622):1417–26. https://doi.org/10.1016/S0140-6736(08)60423-7.

[22] Freiberg MS, Leaf DA, Goulet JL, et al. The association between the receipt of lipid lowering therapy and HIV status among veterans who met NCEP/ATP III criteria for the receipt of lipid lowering medication. J Gen Intern Med 2009;24(3):334–40. https://doi.org/10.1007/s11606-008-0891-7.

[23] Freiberg MS, McGinnis KA, Kraemer K, et al. The association between alcohol consumption and prevalent cardiovascular diseases among HIV-infected and HIV-uninfected men. J Acquir Immune Defic Syndr 2010;53(2):247–53. https://doi.org/10.1097/QAI.0b013e3181c6c4b7.

[24] Ladapo JA, Richards AK, DeWitt CM, et al. Disparities in the quality of cardiovascular care between HIV-infected versus HIV-uninfected adults in the united states: a cross-sectional study. J Am Heart Assoc 2017;6(11). https://doi.org/10.1161/JAHA.117.007107.

[25] So-Armah K, Freiberg MS. Cardiovascular disease risk in an aging HIV population: not just a question of biology. Curr Opin HIV AIDS 2014;9(4):346–54. https://doi.org/10.1097/COH.0000000000000065.

[26] Bloomfield GS, Hill CL, Chiswell K, et al. Cardiology encounters for underrepresented racial and ethnic groups with human immunodeficiency virus and borderline cardiovascular disease risk. J Racial Ethn Health Disparities 2024;11(3):1509–19. https://doi.org/10.1007/s40615-023-01627-0.

[27] Muiruri C, Dombeck C, Swezey T, et al. Specialty care referral for underrepresented minorities living with HIV in the United States: experiences, barriers, and facilitators. AIDS Patient Care STDS 2024;38(6):259–66. https://doi.org/10.1089/apc.2024.0066.

[28] Helleberg M, Afzal S, Kronborg G, et al. Mortality attributable to smoking among HIV-1-infected individuals: a nationwide, population-based cohort study. Clin Infect Dis 2013;56(5):727–34. https://doi.org/10.1093/cid/cis933.

[29] Rasmussen LD, Helleberg M, May MT, et al. Myocardial infarction among Danish HIV-infected individuals: population-attributable fractions associated with smoking. Clin Infect Dis 2015;60(9):1415–23. https://doi.org/10.1093/cid/civ013.

[30] CD4+ count-guided interruption of antiretroviral treatment. N Engl J Med 2006;355(22):2283–96. https://doi.org/10.1056/NEJMoa062360.

[31] Lu MT, Ribaudo H, Foldyna B, et al. Effects of pitavastatin on coronary artery disease and inflammatory biomarkers in HIV: mechanistic substudy of the REPRIEVE randomized clinical trial. JAMA Cardiol 2024;9(4):323–34. https://doi.org/10.1001/jamacardio.2023.5661.

[32] Crum-Cianflone N, Roediger MP, Eberly L, et al. Increasing rates of obesity among HIV-infected persons during the HIV epidemic. PLoS One 2010;5(4):e10106. https://doi.org/10.1371/journal.pone.0010106.

[33] Koethe JR, Jenkins CA, Lau B, et al. Rising obesity prevalence and weight gain among adults starting antiretroviral therapy in the United States and Canada. AIDS Res Hum Retroviruses 2016;32(1):50–8. https://doi.org/10.1089/aid.2015.0147.

[34] Tate T, Willig AL, Willig JH, et al. HIV infection and obesity: where did all the wasting go? Antivir Ther 2012;17(7):1281–9. https://doi.org/10.3851/IMP2348.

[35] Amano SU, Cohen JL, Vangala P, et al. Local proliferation of macrophages contributes to obesity-associated adipose tissue inflammation. Cell Metab 2014;19(1):162–71. https://doi.org/10.1016/j.cmet.2013.11.017.

[36] Couturier J, Suliburk JW, Brown JM, et al. Human adipose tissue as a reservoir for memory CD4+ T cells and HIV. AIDS 2015;29(6):667–74. https://doi.org/10.1097/QAD.0000000000000599.

[37] Curat CA, Wegner V, Sengenes C, et al. Macrophages in human visceral adipose tissue: increased accumulation in obesity and a source of resistin and visfatin. Diabetologia 2006;49(4):744–7. https://doi.org/10.1007/s00125-006-0173-z.

[38] Lumeng CN, Bodzin JL, Saltiel AR. Obesity induces a phenotypic switch in adipose tissue macrophage polarization. J Clin Invest 2007;117(1):175–84. https://doi.org/10.1172/JCI29881.

[39] Luo L, Liu M. Adipose tissue in control of metabolism. J Endocrinol 2016;231(3):R77–99. https://doi.org/10.1530/JOE-16-0211.

[40] Sax PE, Erlandson KM, Lake JE, et al. Weight gain following initiation of antiretroviral therapy: risk factors in randomized comparative clinical trials. Clin Infect Dis 2020;71(6):1379–89. https://doi.org/10.1093/cid/ciz999.

[41] Shikuma CM, Gangcuangco LM, Killebrew DA, et al. The role of HIV and monocytes/macrophages in adipose tissue biology. J Acquir Immune Defic Syndr 2014;65(2):151–9. https://doi.org/10.1097/01.qai.0000435599.27727.6c.

[42] Venter WDF, Moorhouse M, Sokhela S, et al. Dolutegravir plus two different prodrugs of tenofovir to treat HIV. N Engl J Med 2019;381(9):803–15. https://doi.org/10.1056/NEJMoa1902824.

[43] Fryar C.D., Carroll M.D., and Afful J.. Prevalence of overweight, obesity, and severe obesity among adults aged 20 and over: United States, 1960–1962 through 2017–2018. 2020 [cited 2024 July 1, 2024]; Available from: https://www.cdc.gov/nchs/data/hestat/obesity-adult-17-18/obesity-adult.htm#table1.

[44] Hasse B, Iff M, Ledergerber B, et al. Obesity trends and body mass index changes after starting antiretroviral treatment: the Swiss HIV cohort study. Open Forum Infect Dis 2014;1(2):ofu040. https://doi.org/10.1093/ofid/ofu040.

[45] Yuh B, Tate J, Butt AA, et al. Weight change after antiretroviral therapy and mortality. Clin Infect Dis 2015;60(12):1852–9. https://doi.org/10.1093/cid/civ192.

[46] Kanters S, Renaud F, Rangaraj A, et al. Evidence synthesis evaluating body weight gain among people treating HIV with antiretroviral therapy - a systematic literature review and network meta-analysis. EClinicalMedicine 2022;48:101412. https://doi.org/10.1016/j.eclinm.2022.101412.

[47] Martinez-Sanz J, Blanco JR, Muriel A, et al. Weight changes after antiretroviral therapy initiation in CoRIS (Spain): a prospective multicentre cohort study. J Int AIDS Soc 2021;24(5):e25732. https://doi.org/10.1002/jia2.25732.

[48] Talathi R, Anekwe CV, Toribio M. Epidemiology of obesity among people with HIV. Curr Opin HIV AIDS 2024;19(1):1–5. https://doi.org/10.1097/COH.0000000000000830.

[49] Bares SH, Smeaton LM, Xu A, et al. HIV-infected women gain more weight than HIV-infected men following the initiation of antiretroviral therapy. J Womens Health 2018;27(9):1162–9. https://doi.org/10.1089/jwh.2017.6717 (Larchmt).

[50] Bakal DR, Coelho LE, Luz PM, et al. Obesity following ART initiation is common and influenced by both traditional and HIV-/ART-specific risk factors. J Antimicrob Chemother 2018;73(8):2177–85. https://doi.org/10.1093/jac/dky145.

[51] Grabar S, Potard V, Piroth L, et al. Striking differences in weight gain after cART initiation depending on early or advanced presentation: results from the ANRS CO4 FHDH cohort. J Antimicrob Chemother 2023;78(3):757–68. https://doi.org/10.1093/jac/dkad007.

[52] Bourgi K, Rebeiro PF, Turner M, et al. Greater weight gain in treatment-naive persons starting dolutegravir-based antiretroviral therapy. Clin Infect Dis 2020;70(7):1267–74. https://doi.org/10.1093/cid/ciz407.

[53] Menard A, Meddeb L, Tissot-Dupont H, et al. Dolutegravir and weight gain: an unexpected bothering side effect? AIDS 2017;31(10):1499–500. https://doi.org/10.1097/QAD.0000000000001495.

[54] Rizzardo S, Lanzafame M, Lattuada E, et al. Dolutegravir monotherapy and body weight gain in antiretroviral naive patients. AIDS 2019;33(10):1673–4. https://doi.org/10.1097/QAD.0000000000002245.

[55] Norwood J, Turner M, Bofill C, et al. Brief report: weight gain in persons with HIV switched from efavirenz-based to integrase strand transfer inhibitor-based regimens. J Acquir Immune Defic Syndr 2017;76(5):527–31. https://doi.org/10.1097/QAI.0000000000001525.

[56] Capeau J, Lagathu C, Bereziat V. Recent data on the role of antiretroviral therapy in weight gain and obesity in persons living with HIV. Curr Opin HIV AIDS 2024;19(1):14–20. https://doi.org/10.1097/COH.0000000000000833.

[57] Verburgh ML, Wit F, Boyd A, et al. One in 10 virally suppressed persons with HIV in the Netherlands experiences >/=10% weight gain after switching to tenofovir alafenamide and/or integrase strand transfer inhibitor. Open Forum Infect Dis 2022;9(7):ofac291. https://doi.org/10.1093/ofid/ofac291.

[58] Gervasoni C, Cattaneo D, Di Cristo V, et al. Orlistat: weight lost at cost of HIV rebound. J Antimicrob Chemother 2016;71(6):1739–41. https://doi.org/10.1093/jac/dkw033.

[59] Kent SJ. Loss of control of HIV viremia associated with the fat malabsorption drug orlistat. AIDS Res Hum Retroviruses 2012;28(9):961–2. https://doi.org/10.1089/AID.2012.0017.

[60] Haidar L, Crane HM, Nance RM, et al. Weight loss associated with semaglutide treatment among people with HIV. AIDS 2024;38(4):531–5. https://doi.org/10.1097/QAD.0000000000003791.

[61] Nguyen Q, Wooten D, Lee D, et al. GLP-1 receptor agonists promote weight loss among people with HIV. Clin Infect Dis 2024. https://doi.org/10.1093/cid/ciae151.

[62] Achila OO, Abrhaley F, Kesete Y, et al. Dyslipidemia and associated risk factors among HIV/AIDS patients on HAART in Asmara, Eritrea. PLoS One 2022;17(7):e0270838. https://doi.org/10.1371/journal.pone.0270838.

[63] Thompson MA, Horberg MA, Agwu AL, et al. Primary Care Guidance for Persons With Human Immunodeficiency Virus: 2020 Update by the HIV Medicine Association of the Infectious Diseases Society of America. Clin Infect Dis 2021;73(11):e3572–605. https://doi.org/10.1093/cid/ciaa1391.

[64] Jensen MD, Ryan DH, Apovian CM, et al. 2013 AHA/ACC/TOS guideline for the management of overweight and obesity in adults: a report of the American college of cardiology/American heart association task force on practice guidelines and the obesity society. Circulation 2014;129(25 Suppl 2):S102–38. https://doi.org/10.1161/01.cir.0000437739.71477.ee.

[65] Ambrosioni J, Levi L, Alagaratnam J, et al. Major revision version 12.0 of the European AIDS clinical society guidelines 2023. HIV Med 2023;24(11):1126–36. https://doi.org/10.1111/hiv.13542.

[66] Blodget E, Shen C, Aldrovandi G, et al. Relationship between microbial translocation and endothelial function in HIV infected patients. PLoS One 2012;7(8):e42624. https://doi.org/10.1371/journal.pone.0042624.

[67] Chu C, Selwyn PA. Complications of HIV infection: a systems-based approach. Am Fam Physician 2011;83(4):395–406.

[68] Fahme SA, Bloomfield GS, Peck R. Hypertension in HIV-infected adults: novel pathophysiologic mechanisms. Hypertension 2018;72(1):44–55. https://doi.org/10.1161/HYPERTENSIONAHA.118.10893.

[69] Manner IW, Baekken M, Kvale D, et al. Markers of microbial translocation predict hypertension in HIV-infected individuals. HIV Med 2013;14(6):354–61. https://doi.org/10.1111/hiv.12015.

[70] Srinivasa S, Fitch KV, Wong K, et al. RAAS activation is associated with visceral adiposity and insulin resistance among HIV-infected patients. J Clin Endocrinol Metab 2015;100(8):2873–82. https://doi.org/10.1210/jc.2015-1461.

[71] Haile M, Degelo T, Adilo TM, et al. Prevalence of hypertension and its associated factors among adults living with HIV on antiretroviral treatment in selected public hospitals in addis Ababa, Ethiopia. HIV AIDS 2024;16:109–22. https://doi.org/10.2147/HIV.S447396 (Auckl).

[72] Xu X, Chen X, Lin H, et al. General and abdominal obesity and incident hypertension among people living with HIV on antiretroviral therapy. AIDS Care 2021;33(12):1616–20. https://doi.org/10.1080/09540121.2020.1852158.

[73] van Zoest RA, van den Born BH, Reiss P. Hypertension in people living with HIV. Curr Opin HIV AIDS 2017;12(6):513–22. https://doi.org/10.1097/COH.0000000000000406.

[74] Peck RN, Shedafa R, Kalluvya S, et al. Hypertension, kidney disease, HIV and antiretroviral therapy among Tanzanian adults: a cross-sectional study. BMC Med 2014;12:125. https://doi.org/10.1186/s12916-014-0125-2.

[75] Medina-Torne S, Ganesan A, Barahona I, et al. Hypertension is common among HIV-infected persons, but not associated with HAART. J Int Assoc Physicians AIDS Care 2012;11(1):20–5. https://doi.org/10.1177/1545109711418361 (Chic).

[76] Denu MKI, Revoori R, Buadu MAE, et al. Hypertension among persons living with HIV/AIDS and its association with HIV-related health factors. AIDS Res Ther 2024;21(1):5. https://doi.org/10.1186/s12981-023-00576-2.

[77] Xu Y, Chen X, Wang K. Global prevalence of hypertension among people living with HIV: a systematic review and meta-analysis. J Am Soc Hypertens 2017;11(8):530–40. https://doi.org/10.1016/j.jash.2017.06.004.

[78] Davis K, Perez-Guzman P, Hoyer A, et al. Association between HIV infection and hypertension: a global systematic review and meta-analysis of cross-sectional studies. BMC Med 2021;19(1):105. https://doi.org/10.1186/s12916-021-01978-7.

[79] Oyawa I, Adhiambo M, Wesonga B, et al. Burden of hypertension and associated factors among HIV-positive adults in Busia County, Kenya. Pan Afr Med J 2022;43:143. https://doi.org/10.11604/pamj.2022.43.143.36394.

[80] Mogaka JN, Sharma M, Temu T, et al. Prevalence and factors associated with hypertension among adults with and without HIV in Western Kenya. PLoS One 2022;17(1):e0262400. https://doi.org/10.1371/journal.pone.0262400.

[81] Tegegne KD, Adela GA, Kassie GA, et al. Prevalence and factors associated with hypertension among peoples living with HIV in East Africa, a systematic review and meta-analysis. BMC Infect Dis 2023;23(1):724. https://doi.org/10.1186/s12879-023-08679-x.

[82] Kavishe BB, Olsen MF, Filteau S, et al. Blood pressure and body composition during first year of antiretroviral therapy in people with HIV compared With HIV-uninfected community controls. Am J Hypertens 2022;35(11):929–37. https://doi.org/10.1093/ajh/hpac085.

[83] Gelpi M, Karvig LU, Knudsen AD, et al. Incidence of hypertension in people with HIV infection: a longitudinal observational study. AIDS 2023;37(11):1705–9. https://doi.org/10.1097/QAD.0000000000003609.

[84] Gelpi M, Afzal S, Lundgren J, et al. Higher risk of abdominal obesity, elevated low-density lipoprotein cholesterol, and hypertriglyceridemia, but not of hypertension, in people living with human immunodeficiency virus (HIV): results from the copenhagen comorbidity in HIV infection study. Clin Infect Dis 2018;67(4):579–86. https://doi.org/10.1093/cid/ciy146.

[85] Mancia G, Kreutz R, Brunstrom M, et al. 2023 ESH guidelines for the management of arterial hypertension the task force for the management of arterial hypertension of the European society of hypertension: endorsed by the international society of hypertension (ISH) and the European renal association (ERA). J Hypertens 2023;41(12):1874–2071. https://doi.org/10.1097/HJH.0000000000003480.

[86] Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: A report of the american college of cardiology/American heart association task force on clinical practice guidelines. J Am Coll Cardiol 2018;71(19):e127–248. https://doi.org/10.1016/j.jacc.2017.11.006.

[87] Kalra S, Agrawal N. Diabetes and HIV: current understanding and future perspectives. Curr Diab Rep 2013;13(3):419–27. https://doi.org/10.1007/s11892-013-0369-9.

[88] Paik IJ, Kotler DP. The prevalence and pathogenesis of diabetes mellitus in treated HIV-infection. Best Pract Res Clin Endocrinol Metab 2011;25(3):469–78. https://doi.org/10.1016/j.beem.2011.04.003.

[89] Justman JE, Benning L, Danoff A, et al. Protease inhibitor use and the incidence of diabetes mellitus in a large cohort of HIV-infected women. J Acquir Immune Defic Syndr 2003;32(3):298–302. https://doi.org/10.1097/00126334-200303010-00009.

[90] Tien PC, Schneider MF, Cole SR, et al. Antiretroviral therapy exposure and incidence of diabetes mellitus in the Women's Interagency HIV Study. AIDS 2007;21(13):1739–45. https://doi.org/10.1097/QAD.0b013e32827038d0.

[91] Tien PC, Schneider MF, Cox C, et al. Association of HIV infection with incident diabetes mellitus: impact of using hemoglobin A1C as a criterion for diabetes. J Acquir Immune Defic Syndr 2012;61(3):334–40. https://doi.org/10.1097/QAI.0b013e31826bfc32.

[92] Brown TT, Cole SR, Li X, et al. Antiretroviral therapy and the prevalence and incidence of diabetes mellitus in the multicenter AIDS cohort study. Arch Intern Med 2005;165(10):1179–84. https://doi.org/10.1001/archinte.165.10.1179.

[93] Ledergerber B, Furrer H, Rickenbach M, et al. Factors associated with the incidence of type 2 diabetes mellitus in HIV-infected participants in the Swiss HIV Cohort Study. Clin Infect Dis 2007;45(1):111–9. https://doi.org/10.1086/518619.

[94] De Wit S, Sabin CA, Weber R, et al. Incidence and risk factors for new-onset diabetes in HIV-infected patients: the data collection on adverse events of anti-HIV drugs (D:A:D) study. Diabetes Care 2008;31(6):1224–9. https://doi.org/10.2337/dc07-2013.

[95] Hernandez-Romieu AC, Garg S, Rosenberg ES, et al. Is diabetes prevalence higher among HIV-infected individuals compared with the general population? Evidence from MMP and NHANES 2009-2010. BMJ Open Diabetes Res Care, 5; 2017, e000304. https://doi.org/10.1136/bmjdrc-2016-000304.

[96] Njuguna B, Kiplagat J, Bloomfield GS, et al. Prevalence, risk factors, and pathophysiology of dysglycemia among people living with HIV in sub-Saharan Africa. J Diabetes Res 2018:6916497. https://doi.org/10.1155/2018/6916497.

[97] Herrin M, Tate JP, Akgun KM, et al. Weight gain and incident diabetes among HIV-infected veterans initiating antiretroviral therapy compared with uninfected individuals. J Acquir Immune Defic Syndr 2016;73(2):228–36. https://doi.org/10.1097/QAI.0000000000001071.

[98] Tripathi A, Liese AD, Jerrell JM, et al. Incidence of diabetes mellitus in a population-based cohort of HIV-infected and non-HIV-infected persons: the impact of clinical and therapeutic factors over time. Diabet Med 2014;31(10):1185–93. https://doi.org/10.1111/dme.12455.

[99] Capeau J, Bouteloup V, Katlama C, et al. Ten-year diabetes incidence in 1046 HIV-infected patients started on a combination antiretroviral treatment. AIDS 2012;26(3):303–14. https://doi.org/10.1097/QAD.0b013e32834e8776.

[100] Hirigo AT, Gutema S, Eifa A, et al. Experience of dolutegravir-based antiretroviral treatment and risks of diabetes mellitus. SAGE Open Med Case Rep 2022;10. https://doi.org/10.1177/2050313×221079444.

[101] Nduka CU, Stranges S, Kimani PK, et al. Is there sufficient evidence for a causal association between antiretroviral therapy and diabetes in HIV-infected patients?

A meta-analysis. Diabetes Metab Res Rev 2017;33(6). https://doi.org/10.1002/dmrr.2902.
[102] Spagnuolo V, Galli L, Poli A, et al. Associations of statins and antiretroviral drugs with the onset of type 2 diabetes among HIV-1-infected patients. BMC Infect Dis 2017;17(1):43. https://doi.org/10.1186/s12879-016-2099-5.
[103] Eckhardt BJ, Holzman RS, Kwan CK, et al. Glycated Hemoglobin A(1c) as screening for diabetes mellitus in HIV-infected individuals. AIDS Patient Care STDS 2012;26(4):197–201. https://doi.org/10.1089/apc.2011.0379.
[104] Kim PS, Woods C, Georgoff P, et al. A1C underestimates glycemia in HIV infection. Diabetes Care 2009;32(9):1591–3. https://doi.org/10.2337/dc09-0177.
[105] Slama L, Palella Jr FJ, Abraham AG, et al. Inaccuracy of haemoglobin A1c among HIV-infected men: effects of CD4 cell count, antiretroviral therapies and haematological parameters. J Antimicrob Chemother 2014;69(12):3360–7. https://doi.org/10.1093/jac/dku295.
[106] Diop ME, Bastard JP, Meunier N, et al. Inappropriately low glycated hemoglobin values and hemolysis in HIV-infected patients. AIDS Res Hum Retroviruses 2006;22(12):1242–7. https://doi.org/10.1089/aid.2006.22.1242.
[107] Polgreen PM, Putz D, Stapleton JT. Inaccurate glycosylated hemoglobin A1C measurements in human immunodeficiency virus-positive patients with diabetes mellitus. Clin Infect Dis 2003;37(4):e53–6. https://doi.org/10.1086/376633.
[108] American diabetes association professional practice, C., 2. Classification and diagnosis of diabetes: standards of medical care in diabetes-2022. Diabetes Care 2022;45(Suppl 1):S17–38. https://doi.org/10.2337/dc22-S002.
[109] Rinella ME, Neuschwander-Tetri BA, Siddiqui MS, et al. AASLD practice guidance on the clinical assessment and management of nonalcoholic fatty liver disease. Hepatology 2023;77(5):1797–835. https://doi.org/10.1097/HEP.0000000000000323.
[110] Price JC, Wang R, Seaberg EC, et al. The association of inflammatory markers with nonalcoholic fatty liver disease differs by human immunodeficiency virus serostatus. Open Forum Infect Dis 2017;4(3):ofx153. https://doi.org/10.1093/ofid/ofx153.
[111] Franco S, Horneros J, Soldevila L, et al. Single nucleotide polymorphisms in PNPLA3, ADAR-1 and IFIH1 are associated with advanced liver fibrosis in patients co-infected with HIV-1//hepatitis C virus. AIDS 2021;35(15):2497–502. https://doi.org/10.1097/QAD.0000000000003066.
[112] Zhang J, Ma S, Zhou W, et al. Genetic polymorphisms of CYP2B6 is a risk of metabolic associated fatty liver disease in Chinese population. Toxicol Appl Pharmacol 2023;481:116770. https://doi.org/10.1016/j.taap.2023.116770.
[113] Puoti M, Nasta P, Gatti F, et al. HIV-related liver disease: ARV drugs, coinfection, and other risk factors. J Int Assoc Physicians AIDS Care (Chic) 2009;8(1):30–42. https://doi.org/10.1177/1545109708330906.
[114] Soriano V, Puoti M, Garcia-Gasco P, et al. Antiretroviral drugs and liver injury. AIDS 2008;22(1):1–13. https://doi.org/10.1097/QAD.0b013e3282f0e2fd.
[115] Bauer KC, Littlejohn PT, Ayala V, et al. Nonalcoholic fatty liver disease and the gut-liver axis: exploring an undernutrition perspective. Gastroenterology 2022;162(7):1858–75. https://doi.org/10.1053/j.gastro.2022.01.058. e2.
[116] Hsu CL, Wang Y, Duan Y, et al. Differences in bacterial translocation and liver injury in ethanol versus diet-induced liver disease. Dig Dis Sci 2023;68(7):3059–69. https://doi.org/10.1007/s10620-023-07860-1.
[117] Seth A, Sherman KE. Fatty liver disease in persons with HIV infection. Top Antivir Med 2019;27(2):75–82.
[118] Sharpton SR, Ajmera V, Loomba R. Emerging role of the gut microbiome in nonalcoholic fatty liver disease: from composition to function. Clin Gastroenterol Hepatol 2019;17(2):296–306. https://doi.org/10.1016/j.cgh.2018.08.065.
[119] Romeo S, Kozlitina J, Xing C, et al. Genetic variation in PNPLA3 confers susceptibility to nonalcoholic fatty liver disease. Nat Genet 2008;40(12):1461–5. https://doi.org/10.1038/ng.257.
[120] Wegermann K, Moylan C, Naggie S. Fatty liver disease: enter the metabolic era. Curr HIV AIDS Rep 2023;20(6):405–18. https://doi.org/10.1007/s11904-023-00669-7.
[121] Sim JH, Sherman JB, Stanley TL, et al. Pro-inflammatory interleukin-18 is associated with hepatic steatosis and elevated liver enzymes in people with HIV monoinfection. AIDS Res Hum Retroviruses 2021;37(5):385–90. https://doi.org/10.1089/AID.2020.0177.
[122] Michel M, Labenz C, Armandi A, et al. Metabolic dysfunction-associated fatty liver disease in people living with HIV. Sci Rep 2023;13(1):9158. https://doi.org/10.1038/s41598-023-32965-y.
[123] Chew KW, Wu K, Tassiopoulos K, et al. Liver inflammation is common and linked to metabolic derangements in persons with treated human immunodeficiency virus (HIV). Clin Infect Dis 2023;76(3):e571–9. https://doi.org/10.1093/cid/ciac708.
[124] Riebensahm C, Berzigotti A, Surial B, et al. Factors associated with liver steatosis in people with human immunodeficiency virus on contemporary antiretroviral therapy. Open Forum Infect Dis 2022;9(11):ofac538. https://doi.org/10.1093/ofid/ofac538.
[125] Gawrieh S, Lake JE, Debroy P, et al. Burden of fatty liver and hepatic fibrosis in persons with HIV: A diverse cross-sectional US multicenter study. Hepatology 2023;78(2):578–91. https://doi.org/10.1097/HEP.0000000000000313.
[126] Price J, Ma Y, Adimora A, et al. Multisite prospective liver disease and reproductive ageing (LIVRA) study in US women living with and without HIV. BMJ Open 2022;12(4):e055706. https://doi.org/10.1136/bmjopen-2021-055706.
[127] Kalligeros M, Vassilopoulos A, Shehadeh F, et al. Prevalence and characteristics of nonalcoholic fatty liver disease and fibrosis in people living With HIV Monoinfection: A systematic review and meta-analysis. Clin Gastroenterol Hepatol 2023;21(7):1708–22. https://doi.org/10.1016/j.cgh.2023.01.001.
[128] Maurice JB, Patel A, Scott AJ, et al. Prevalence and risk factors of nonalcoholic fatty liver disease in HIV-monoinfection. AIDS 2017;31(11):1621–32. https://doi.org/10.1097/QAD.0000000000001504.
[129] Krishnan A, Sims OT, Surapaneni PK, et al. Risk of adverse cardiovascular outcomes among people with HIV and nonalcoholic fatty liver disease. AIDS 2023;37(8):1209–16. https://doi.org/10.1097/QAD.0000000000003537.
[130] Guaraldi G, Squillace N, Stentarelli C, et al. Nonalcoholic fatty liver disease in HIV-infected patients referred to a metabolic clinic: prevalence, characteristics, and predictors. Clin Infect Dis 2008;47(2):250–7. https://doi.org/10.1086/589294.
[131] Jin D, Jin S, Zhou T, et al. Regional variation in NAFLD prevalence and risk factors among people living with HIV in Europe: a meta-analysis. Front Public Health 2023;11:1295165. https://doi.org/10.3389/fpubh.2023.1295165.
[132] Crum-Cianflone N, Dilay A, Collins G, et al. Nonalcoholic fatty liver disease among HIV-infected persons. J Acquir Immune Defic Syndr 2009;50(5):464–73. https://doi.org/10.1097/QAI.0b013e318198a88a.
[133] Fernandez CJ, Alkhalifah M, Afsar H, et al. Metabolic dysfunction-associated fatty liver disease and chronic viral hepatitis: the interlink. Pathogens 2024;13(1). https://doi.org/10.3390/pathogens13010068.
[134] Tsai PS, Cheng YM, Wang CC, et al. The impact of concomitant hepatitis C virus infection on liver and cardiovascular risks in patients with metabolic-associated fatty liver disease. Eur J Gastroenterol Hepatol 2023;35(11):1278–83. https://doi.org/10.1097/MEG.0000000000002558.
[135] Price JC, Thio CL. Liver disease in the HIV-infected individual. Clin Gastroenterol Hepatol 2010;8(12):1002–12. https://doi.org/10.1016/j.cgh.2010.08.024.
[136] Price JC, Seaberg EC, Latanich R, et al. Risk factors for fatty liver in the multicenter AIDS cohort study. Am J Gastroenterol 2014;109(5):695–704. https://doi.org/10.1038/ajg.2014.32.
[137] Nunez M. Clinical syndromes and consequences of antiretroviral-related hepatotoxicity. Hepatology 2010;52(3):1143–55. https://doi.org/10.1002/hep.23716.
[138] Moyle G. Clinical manifestations and management of antiretroviral nucleoside analog-related mitochondrial toxicity. Clin Ther 2000;22(8):911–36. https://doi.org/10.1016/S0149-2918(00)80064-8. discussion 898.
[139] Benedicto AM, Fuster-Martinez I, Tosca J, et al. NNRTI and liver damage: evidence of their association and the mechanisms involved. Cells 2021;10(7). https://doi.org/10.3390/cells10071687.
[140] Audsley J, Sasadeusz J, Lewin SR. Tesamorelin, liver fat, and NAFLD in the setting of HIV. Lancet HIV 2019;6(12):e808–9. https://doi.org/10.1016/S2352-3018(19)30331-5.
[141] Kositamongkol C, Kanchanasurakit S, Auttamalang C, et al. Coffee consumption and non-alcoholic fatty liver disease: an umbrella review and a systematic review and meta-analysis. Front Pharmacol 2021;12:786596. https://doi.org/10.3389/fphar.2021.786596.
[142] Kamolvisit S, Chirnaksorn S, Nimitphong H, et al. Pioglitazone for the treatment of metabolic-associated fatty liver disease in people living with HIV and prediabetes. Cureus 2021;13(10):e19046. https://doi.org/10.7759/cureus.19046.
[143] Stanley TL, Fourman LT, Feldpausch MN, et al. Effects of tesamorelin on non-alcoholic fatty liver disease in HIV: a randomised, double-blind, multicentre trial. Lancet HIV 2019;6(12):e821–30. https://doi.org/10.1016/S2352-3018(19)30338-8.
[144] Tafesh ZH, Verna EC. Managing nonalcoholic fatty liver disease in patients living with HIV. Curr Opin Infect Dis 2017;30(1):12–20. https://doi.org/10.1097/QCO.0000000000000344.
[145] Guaraldi G, Maurice JB, Marzolini C, et al. New drugs for NASH and HIV infection: great expectations for a great need. Hepatology 2020;71(5):1831–44. https://doi.org/10.1002/hep.31177.
[146] Siegel MO, Borkowska AG, Dubrovsky L, et al. HIV infection induces structural and functional changes in high density lipoproteins. Atherosclerosis 2015;243(1):19–29. https://doi.org/10.1016/j.atherosclerosis.2015.08.036.
[147] Zidar DA, Juchnowski S, Ferrari B, et al. Oxidized LDL levels are increased in HIV infection and may drive monocyte activation. J Acquir Immune Defic Syndr 2015;69(2):154–60. https://doi.org/10.1097/QAI.0000000000000566.
[148] Alsheikh-Ali AA, Kitsios GD, Balk EM, et al. The vulnerable atherosclerotic plaque: scope of the literature. Ann Intern Med 2010;153(6):387–95. https://doi.org/10.7326/0003-4819-153-6-201009210-00272.
[149] Subramanian S, Tawakol A, Burdo TH, et al. Arterial inflammation in patients with HIV. JAMA 2012;308(4):379–86. https://doi.org/10.1001/jama.2012.6698.
[150] Grand M, Bia D, Diaz A. Cardiovascular risk assessment in people living with hiv: a systematic review and meta-analysis of real-life data. Curr HIV Res 2020;18(1):5–18. https://doi.org/10.2174/1570162×17666191212091618.
[151] Assefa A, Abiye AA, Tadesse TA, et al. Prevalence and factors associated with dyslipidemia among people living with HIV/AIDS on follow-up care at a tertiary care hospital in ethiopia: a cross-sectional study. Drug Healthc Patient Saf 2023;15:93–102. https://doi.org/10.2147/DHPS.S395037.
[152] Bijker R, Choi JY, Ditangco R, et al. Cardiovascular disease and cardiovascular disease risk in HIV-positive populations in the asian region. Open AIDS J 2017;11:52–66. https://doi.org/10.2174/1874613601711010052.
[153] Fiseha T, Alemu W, Dereje H, et al. Prevalence of dyslipidaemia among HIV-infected patients receiving combination antiretroviral therapy in North Shewa, Ethiopia. PLoS One 2021;16(4):e0250328. https://doi.org/10.1371/journal.pone.0250328.

[154] Althoff KN, Stewart C, Humes E, et al. The forecasted prevalence of comorbidities and multimorbidity in people with HIV in the United States through the year 2030: A modeling study. PLoS Med 2024;21(1):e1004325. https://doi.org/10.1371/journal.pmed.1004325.
[155] Francisco C, Gonzales E, Yu MG, et al. Metabolic profile of people living with HIV in a treatment hub in manila, philippines: a pre- and post-antiretroviral analysis. J ASEAN Fed Endocr Soc 2022;37(1):53–61. https://doi.org/10.15605/jafes.037.01.17.
[156] Friis-Moller N, Weber R, Reiss P, et al. Cardiovascular disease risk factors in HIV patients–association with antiretroviral therapy. Results from the DAD study. AIDS 2003;17(8):1179–93. https://doi.org/10.1097/01.aids.0000060358.78202.c1.
[157] Woldu MA, Minzi O, Engidawork E. Dyslipidemia and associated cardiovascular risk factors in HIV-positive and HIV-negative patients visiting ambulatory clinics: A hospital-based study. JRSM Cardiovasc Dis 2022;11. https://doi.org/10.1177/20480040221114651.
[158] Yu XD, Huang H, Jiao Y, et al. Incidence and risk factors of hypertriglyceridemia in males with human immunodeficiency virus who are treated with combination antiretroviral therapy: a retrospective cohort study. Lipids Health Dis 2023;22(1):27. https://doi.org/10.1186/s12944-023-01786-3.
[159] Tripathi A, Jerrell JM, Liese AD, et al. Association of clinical and therapeutic factors with incident dyslipidemia in a cohort of human immunodeficiency virus-infected and non-infected adults: 1994-2011. Metab Syndr Relat Disord 2013;11(6):417–26. https://doi.org/10.1089/met.2013.0017.
[160] Dave JA, Levitt NS, Ross IL, et al. Anti-retroviral therapy increases the prevalence of dyslipidemia in South African HIV-infected patients. PLoS One 2016;11(3):e0151911. https://doi.org/10.1371/journal.pone.0151911.
[161] Limas TG, Pinto Gde A, Marcato LM, et al. Analysis of the prevalence of dyslipidemia in individuals with HIV and its association with antiretroviral therapy. Rev Soc Bras Med Trop 2014;47(5):547–51. https://doi.org/10.1590/0037-8682-0128-2014.
[162] Oliveira DPR, Macedo APA, Dos Santos Goncalves M, et al. Dyslipidemia secondary to the use of HAART in adults: a systematic review. Curr Drug Res Rev 2022;14(3):239–46. https://doi.org/10.2174/2589977514666220519165549.
[163] Floris-Moore M, Howard AA, Lo Y, et al. Increased serum lipids are associated with higher CD4 lymphocyte count in HIV-infected women. HIV Med 2006;7(7):421–30. https://doi.org/10.1111/j.1468-1293.2006.00401.x.
[164] Shen Y, Wang J, Wang Z, et al. Prevalence of dyslipidemia among antiretroviral-naive HIV-infected individuals in China. Medicine 2015;94(48):e2201. https://doi.org/10.1097/MD.0000000000002201 (Baltimore).
[165] The RSG. Incidence of dyslipidemia in people with HIV who are treated with integrase inhibitors versus other antiretroviral agents. AIDS 2021;35(6):869–82. https://doi.org/10.1097/QAD.0000000000002811.
[166] Baker JV, Sharma S, Achhra AC, et al. Changes in cardiovascular disease risk factors with immediate versus deferred antiretroviral therapy initiation among HIV-positive participants in the START (Strategic Timing of Antiretroviral Treatment) Trial. J Am Heart Assoc 2017;6(5). https://doi.org/10.1161/JAHA.116.004987.
[167] Gatell JM, Assoumou L, Moyle G, et al. Switching from a ritonavir-boosted protease inhibitor to a dolutegravir-based regimen for maintenance of HIV viral suppression in patients with high cardiovascular risk. AIDS 2017;31(18):2503–14. https://doi.org/10.1097/QAD.0000000000001675.
[168] Kamara DA, Smith C, Ryom L, et al. Longitudinal analysis of the associations between antiretroviral therapy, viraemia and immunosuppression with lipid levels: the D:A:D study. Antivir Ther 2016;21(6):495–506. https://doi.org/10.3851/IMP3051.
[169] Vemulapalli AC, Elias AA, Yerramsetti MD, et al. The impact of contemporary antiretroviral drugs on atherosclerosis and its complications in people living with HIV: a systematic review. Cureus 2023;15(10):e47730. https://doi.org/10.7759/cureus.47730.
[170] Kalra DK, Vorla M, Michos ED, et al. Dyslipidemia in human immunodeficiency virus disease: JACC review topic of the week. J Am Coll Cardiol 2023;82(2):171–81. https://doi.org/10.1016/j.jacc.2023.04.050.
[171] Jacobson TA, Maki KC, Orringer CE, et al. National lipid association recommendations for patient-centered management of dyslipidemia: part 2. J Clin Lipidol 2015;9(6 Suppl). https://doi.org/10.1016/j.jacl.2015.09.002. S1-122 e1.
[172] Panel on antiretroviral guidelines for adults and adolescents. Guidelines for the use of antiretroviral agents in adults and adolescents with HIV. 2024 May 22, 2024]; Available from: https://clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/adult-adolescent-arv/guidelines-adult-adolescent-arv.pdf.
[173] Grinspoon SK, Fitch KV, Zanni MV, et al. Pitavastatin to prevent cardiovascular disease in HIV infection. N Engl J Med 2023;389(8):687–99. https://doi.org/10.1056/NEJMoa2304146.
[174] Faragon J., McGowan J., Fine S., et al. ART drug-drug interactions. 2023 May 22, 2024]; Available from: https://www.hivguidelines.org/wpcontent/uploads/2023/01/NYSDOH-AI-ART-Drug-DrugInteractions_1012-2023_HG.pdf.
[175] University of Liverpool. HIV drug interactions. May 22, 2024; Available from: https://www.hiv-druginteractions.org.
[176] World Health Organization. Updated recommendations on first-line and second-line antiretroviral regimens and post-exposure prophylaxis and recommendations on early infant diagnosis of HIV. 2018 May 22, 2024; Available from: https://iris.who.int/bitstream/handle/10665/277395/WHO-CDS-HIV-18.51-eng.pdf?sequence=1.
[177] D'Agostino RB, Vasan RS, Pencina Sr MJ, et al. General cardiovascular risk profile for use in primary care: the framingham heart study. Circulation 2008;117(6):743–53. https://doi.org/10.1161/CIRCULATIONAHA.107.699579.
[178] Goff DC, Lloyd-Jones DM, Bennett Jr G, et al. 2013 ACC/AHA guideline on the assessment of cardiovascular risk: a report of the American college of cardiology/American heart association task force on practice guidelines. J Am Coll Cardiol 2014;63(25 Pt B):2935–59. https://doi.org/10.1016/j.jacc.2013.11.005.
[179] McGinnis KA, Justice AC, Moore RD, et al. Discrimination and calibration of the veterans aging cohort study index 2.0 for predicting mortality among people with human immunodeficiency virus in North America. Clin Infect Dis 2022;75(2):297–304. https://doi.org/10.1093/cid/ciab883.
[180] Tate JP, Justice AC, Hughes MD, et al. An internationally generalizable risk index for mortality after one year of antiretroviral therapy. AIDS 2013;27(4):563–72. https://doi.org/10.1097/QAD.0b013e32835b8c7f.
[181] Soares C, Kwok M, Boucher KA, et al. Performance of cardiovascular risk prediction models among people living With HIV: a systematic review and meta-analysis. JAMA Cardiol 2023;8(2):139–49. https://doi.org/10.1001/jamacardio.2022.4873.
[182] Feinstein MJ, Nance RM, Drozd DR, et al. Assessing and refining myocardial infarction risk estimation among patients with human immunodeficiency virus: a study by the centers for AIDS research network of integrated clinical systems. JAMA Cardiol 2017;2(2):155–62. https://doi.org/10.1001/jamacardio.2016.4494.
[183] Thompson-Paul AM, Lichtenstein KA, Armon C, et al. Cardiovascular disease risk prediction in the HIV outpatient study. Clin Infect Dis 2016;63(11):1508–16. https://doi.org/10.1093/cid/ciw615.
[184] Triant VA, Perez J, Regan S, et al. Cardiovascular risk prediction functions underestimate risk in HIV infection. Circulation 2018;137(21):2203–14. https://doi.org/10.1161/CIRCULATIONAHA.117.028975.
[185] Lichtenstein KA, Armon C, Buchacz K, et al. Low CD4+ T cell count is a risk factor for cardiovascular disease events in the HIV outpatient study. Clin Infect Dis 2010;51(4):435–47. https://doi.org/10.1086/655144.
[186] Chow FC, Bacchetti P, Kim AS, et al. Effect of CD4+ cell count and viral suppression on risk of ischemic stroke in HIV infection. AIDS 2014;28(17):2573–7. https://doi.org/10.1097/QAD.0000000000000452.
[187] Alvaro-Meca A, Berenguer J, Diaz A, et al. Stroke in HIV-infected individuals with and without HCV coinfection in Spain in the combination antiretroviral therapy era. PLoS One 2017;12(6):e0179493. https://doi.org/10.1371/journal.pone.0179493.
[188] McKibben RA, Haberlen SA, Post WS, et al. A cross-sectional study of the association between chronic hepatitis C virus infection and subclinical coronary atherosclerosis among participants in the multicenter AIDS cohort study. J Infect Dis 2016;213(2):257–65. https://doi.org/10.1093/infdis/jiv396.
[189] Karady J, Lu MT, Bergstrom G, et al. Coronary plaque in people with HIV vs non-HIV asymptomatic community and symptomatic higher-risk populations. JACC Adv 2024;3(6):100968. https://doi.org/10.1016/j.jacadv.2024.100968.
[190] Jensen MD, Ryan DH, Apovian CM, et al. 2013 AHA/ACC/TOS guideline for the management of overweight and obesity in adults: a report of the American College of cardiology/American heart association task force on practice guidelines and the obesity society. J Am Coll Cardiol 2014;63(25 Pt B):2985–3023. https://doi.org/10.1016/j.jacc.2013.11.004.
[191] American Diabetes Association Professional Practice, C., 6. Glycemic targets: standards of medical care in diabetes-2022. Diabetes Care 2022;45(Suppl 1):S83–96. https://doi.org/10.2337/dc22-S006.
[192] Abushamat LA, Shah PA, Eckel RH, et al. The emerging role of glucagon-like peptide-1 receptor agonists for the treatment of metabolic dysfunction-associated steatohepatitis. Clin Gastroenterol Hepatol 2024. https://doi.org/10.1016/j.cgh.2024.01.032.
[193] Lincoff AM, Brown-Frandsen K, Colhoun HM, et al. Semaglutide and cardiovascular outcomes in obesity without diabetes. N Engl J Med 2023;389(24):2221–32. https://doi.org/10.1056/NEJMoa2307563.
[194] Kosiborod MN, Abildstrom SZ, Borlaug BA, et al. Semaglutide in patients with heart failure with preserved ejection fraction and obesity. N Engl J Med 2023;389(12):1069–84. https://doi.org/10.1056/NEJMoa2306963.