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REVIEW

Pathogenesis of HIV-Associated Metabolic Syndrome and Clinical Management Recommendations

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Abstract: The phenomenon of metabolic syndrome in patients with HIV infection has attracted increasing attention. HIV infection increases the risk of metabolic complications, including cardiovascular diseases and diabetes. Meanwhile, the potential metabolic side effects of antiretroviral therapy in HIV patients have emerged as a new clinical challenge. This study delineates the potential mechanisms underlying HIV-associated metabolic syndrome, encompassing inflammation and immune activation, glucose and lipid metabolism disorders, mitochondrial and vascular endothelial abnormalities, gut microbiota dysbiosis, epigenetic alterations, and the application of certain antiretroviral drugs. These mechanisms interact and exacerbate each other, with inflammation and immune activation playing a pivotal role. This study also discusses the potential associations between HIV infection and various metabolic diseases, and consolidates clinical management recommendations for HIV-associated metabolic syndrome, including diet, exercise, and lipid, glucose, and blood pressure management.

Keywords: HIV, metabolic syndrome, antiretroviral therapy, pathogenesis, management strategy

Introduction

Human Immunodeficiency Virus (HIV) infection is a global public health issue. According to the latest data, 40.8 million people were living with HIV (PLWH) globally and 31.6 million people were accessing antiretroviral therapy (ART) in 2024.[1] With the widespread application of highly active antiretroviral therapy (HAART), the survival rate of PLWH has significantly improved,[2] and the causes of death threatening elderly PLWH have gradually shifted from AIDS-related mortality to metabolic diseases, such as cardiovascular diseases.[3] Consequently, HIV-associated metabolic syndrome (HIV-MetS) has emerged as a major focus in current research and clinical practice.[2] The development of metabolic syndrome (MetS) in PLWH leads to diminished quality of life, increased financial burden, and heightened psychological distress. It also significantly elevates the incidence of diabetes and cardiovascular diseases, as well as non-HIV-related mortality, substantially compromising their life expectancy.[4–6]

Metabolic syndrome (MetS) is a cluster of interrelated metabolic abnormalities, including abdominal obesity, insulin resistance, hyperglycemia, hypertension, and dyslipidemia. This condition is significantly associated with an elevated risk of developing cardiovascular diseases (CVD), type 2 diabetes mellitus (T2DM), nonalcoholic fatty liver disease (NAFLD), and other related disorders.[7–11] There are multiple diagnostic criteria for MetS internationally[12] (Table 1).[12–15] But they generally rely on five key components: increased waist circumference, elevated blood pressure, elevated fasting or postprandial glucose, elevated serum triglycerides (TG), and reduced high-density lipoprotein (HDL) cholesterol levels.

Studies have found that PLWH have a higher risk of developing MetS compared to the general population, with an average prevalence of approximately 30%.[16–20] Prevalence varies significantly across regions; for example, in the Americas, it ranges from about 15% to 30%,[5,21,22] in Asia from approximately 10% to 33%,[23–28] and in Africa, it is the highest and most variable, ranging from 5.5% to 58%.[29–31] In sub-Saharan countries with lower economic levels, prevalence is markedly higher than in other African regions .[21,32] With increasing age, the prevalence of HIV-associated MetS gradually rises, and female PLWH are generally considered to have a higher prevalence than males.[33–36] These findings indicate that the prevalence of HIV-MetS is influenced by factors such as age, gender, geographical location,

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Table 1 Diagnostic Criteria for Metabolic Syndrome

Criteria	NCEP/ATP III	IDF	Harmonized	CDS
Elevated waist circumference	Males≥102 cm, females≥88 cm	Europids: males≥94 cm, females≥80cm	Population- and country-specific definitions	Chinese: males≥90 cm, females≥80 cm
Elevated triglycerides	≥1.7 mmol/L, or have received lipid-lowering treatment			
Reduced HDL-C	Males <1.0 mmol/L (40 mg/dL), females <1.3 mmol/L (50 mg/dL), or have received treatment			
Elevated blood pressure	Systolic ≥130 and/or diastolic ≥85 mm Hg, or received antihypertensive drugs			
Elevated fasting glucose	≥5.6 mmol/L (100 mg/dL), or diagnosed diabetes			≥5.5 mmol/L, diagnosed diabetes
Mets can be diagnosed if 3 or more of the above 5 conditions are met.				

Abbreviation: HDL-C, High-Density Lipoprotein Cholesterol.

ethnicity, economic status, and medical resources. Therefore, in general, elderly and female HIV patients, those living in areas with underdeveloped medical resources, and those of African descent require more attention.

The pathogenesis of HIV-MetS primarily involves inflammation and immune activation induced by HIV infection and ART drugs, dyslipidemia, insulin resistance, mitochondrial dysfunction, gut microbiota dysbiosis, epigenetic alterations, and so on.[37,38] Among these, gut microbiota dysbiosis is a relatively new research topic; it causes sustained inflammation and immune activation through mechanisms such as microbial translocation, endotoxemia, and reduction in anti-inflammatory microbiota, thereby affecting metabolism. The mechanisms of epigenetic alterations may be related to dysregulation of histone modifications, immune function, and cellular senescence. Specific antiretroviral drugs are independent risk factors for HIV-MetS;[29] among them, protease inhibitors (PIs) directly affect lipid metabolism and insulin resistance, significantly increasing triglycerides and LDL levels, while nucleoside reverse transcriptase inhibitors (NRTIs) can cause hyperlactatemia, abnormal fat distribution, and hypophosphatemia. The underlying mechanisms require further investigation.

Understanding the specific underlying mechanisms of HIV-MetS is particularly crucial for future treatment, management, and prevention of this condition. However, current research on the mechanisms of HIV-MetS remains limited, and there is a deficiency of effective therapeutic management strategies and optimal lifestyle interventions. Concurrently, the clinical management of metabolic syndrome in this special population also faces significant challenges.

This article focuses on reviewing recent advances in the potential mechanisms underlying HIV-MetS and exploring possible relationships between HIV infection and MetS. We summarize diagnostic criteria for MetS and briefly discuss clinical management and therapeutic recommendations for PLWH with comorbid MetS. This aims to provide insights for improved prevention and treatment of HIV-MetS. Notably, these studies predominantly focus on adult populations, lacking valid data on children living with HIV; therefore, the scope of this review is confined to adults living with HIV.

The Impact of HIV Infection on Multiple Metabolic Diseases

HIV infection and HAART can elevate the risk of developing MetS, thereby increasing the likelihood of progression to neurological disorders (dementia, stroke, etc)., CVD (hypertension, coronary artery disease, etc)., T2DM, and NAFLD. These comorbidities profoundly compromise the quality of life and survival rates among PLWH.

HIV Infection and Cardiovascular Diseases

Studies over recent decades have confirmed that PLWH face a 1.5- to 2-fold increased risk of CVD compared to the general population.[3,39–41] CVD in PLWH encompasses hypertension, cardiomyopathy, heart failure, and coronary artery disease (CAD). A large-scale cohort study has revealed that PLWH exhibit a high prevalence of CAD and a significantly increased burden of coronary plaque.[42] PLWH are 4.5 times as likely to die of sudden cardiac death as the control

group.[43] Research on HIV-associated cardiomyopathy has also indicated that PLWH are at a higher risk of developing coronary artery disease and post-myocardial infarction heart failure.[44] Hypertension is prevalent among PLWH. An Italian multicenter study reported that approximately 30% of adult HIV outpatients had hypertension, while the prevalence surged to as high as 96% in PLWH comorbid with MetS.[45] A global meta-analysis revealed that the prevalence of hypertension in PLWH ranges from 16.5% to 28.1%.[46] Mechanisms such as activation of the renin-angiotensin-aldosterone system (RAAS), monocyte/macrophage activation, and endothelial dysfunction may contribute to the development and progression of cardiovascular diseases in PLWH.[19,47]

HIV Infection and Nervous System Diseases

The impact of HIV infection on the central nervous system is multifaceted, encompassing direct viral invasion, indirect immune system dysfunction, and cerebrovascular accidents induced by concurrent metabolic syndrome .[48–53] Common neurological disorders include cognitive impairment, psychological issues, dementia, and cerebrovascular disease.[54] Studies have demonstrated that HIV infection allows the virus to cross the blood-brain barrier and invade the central nervous system, leading to a range of neurological complications such as behavioral abnormalities, motor dysfunction, and HIV-associated dementia (HAD) .[48] A meta-analysis indicates a heightened prevalence of stroke among people living with HIV (PLWH), particularly in older age groups.[55] Furthermore, HIV infection may independently increase the risk of stroke,[52] with pathogenesis closely linked to HIV-induced vasculitis, immune dysregulation, ART side effects, and metabolic disorders.

HIV Infection and NAFLD

Among PLWH, chronic liver disease is the second leading cause of non-HIV-related death.[56] HIV accelerates the progression of PLWH to MetS by impairing adipokine synthesis and further promotes the development of HIV-associated fatty liver disease (HIV-ALD) through liver-specific mediators.[57–59] A 2018 cross-sectional study in Brazil showed that the prevalence of hepatic steatosis among PLWH was 35%;[60] A 2023 meta-analysis reported even higher rates of HIV-ALD, with prevalence rates of non-alcoholic steatohepatitis (NASH) and hepatic fibrosis at 48.77% and 23.34%.[9] The prevalence of HIV-ALD varies across regions, but overall, PLWH is more susceptible to developing hepatic steatosis compared to the general population.[61] Once hepatic steatosis occurs, PLWH faces a heightened risk of progression to fibrosis.[56,62,63]

HIV Infection and T2DM

Although T2DM has been extensively documented among PLWH ,[64] research on the relationship and underlying mechanisms between HIV and diabetes remains limited, with ongoing debates regarding their epidemiological association. Studies have demonstrated that PLWH and those receiving ART exhibit a significantly elevated risk of developing prediabetes and diabetes mellitus compared to the general population.[65–68] However, other research suggests that HIV-specific factors may not independently contribute to increased diabetes prevalence, with conventional risk factors such as aging, obesity, and metabolic abnormalities playing a more dominant role.[69,70] In summary, the majority of research still leans toward the conclusion that HIV and ART play a modest role in predisposing affected populations to diabetes,[71,72] particularly among elderly patients and those with hyperlipidemia.[73,74] The mechanisms likely involve chronic inflammation,[75] insulin resistance, and impaired glucose metabolism.[76,77] The latest HIV clinical guidelines issued by the National Institutes of Health (NIH) recommend routine blood glucose testing before ART, which indirectly highlights the potential role of HIV in the development and progression of diabetes mellitus.[64]

HIV Infection and Other Non-HIV Comorbidities

PLWH also develop comorbidities such as osteoporosis,[78] fractures,[79] and non-AIDS-defining cancers (NADCs).[80–82] These may all be related to aging.The phenomenon of aging in PLWH was observed decades ago.[83] PLWH exhibit significant biological age acceleration. Epigenetic studies indicate that their biological age is, on average, 4.9–14.7 years older than their chronological age.[84] Moreover, PLWH develop age-related comorbidities—such as coronary artery disease (CAD), cancer, osteoporosis, and frailty syndrome—approximately 10–15 years earlier than HIV-uninfected individuals.[85]

Even early initiation of antiretroviral therapy (ART) fails to prevent these complications[79] fully. Literature has described the aging phenomena in HIV disease (including cellular senescence and immunosenescence), which may be associated with declining immune system functions (such as reduced innate immune cell functionality, decreased CD4+/CD8+ T-cell ratio), chronic inflammation, epigenetic alterations, and metabolic dysregulation.[85–89]

All these confirm that PLWH are at greater risk of developing various metabolic diseases (Figure 1), and there is an urgent need to clarify the pathogenesis and develop effective management strategies.

Pathogenic Mechanisms of HIV-Associated Metabolic Syndrome

The pathogenesis of HIV-MetS is complex and remains incompletely elucidated. Currently, several hypotheses exist regarding the pathogenesis of HIV-MetS (Table 2), but these are relatively fragmented. Our analysis of existing data indicates that the development of HIV-MetS involves synergistic interactions of multiple factors, including chronic inflammation and immune activation, mitochondrial dysfunction, abnormalities in glucose and lipid metabolism, mitochondrial and vascular endothelial abnormalities, intestinal dysbiosis, epigenetic modifications, and the use of antiretroviral drugs (Figure 1).

Chronic Inflammation and Immune Dysregulation

HIV infection is a complex systemic disease characterized by chronic inflammation and persistent immune activation. Its key features include elevated levels of multiple pro-inflammatory cytokines (such as tumor necrosis factor-α (TNF-α), integrin-αM, interferon-α (IFN-α), interleukin-6 (IL-6), and interleukin-1β (IL-1β)), activation of immune cells, alterations in other immunologically active substances, and increased coagulation biomarkers.[90,91] It is well known that adipose tissue serves as a reservoir for HIV and is abundant in immune cells, such as CD4+ T cells and macrophages.[92] Following HIV infection, the virus triggers the release of substantial cytokines that induce oxidative stress responses, mitochondrial dysfunction, inflammatory alterations, and apoptosis in adipocytes. On the one hand, these alterations lead to adipose tissue dysfunction, exacerbating the release of inflammatory cytokines, impairing adiponectin function, and compromising insulin signaling in skeletal muscles, thereby inducing a cascade of metabolic disorders such as hypertriglyceridemia and systemic insulin resistance. On the other hand, they provoke vascular endothelial damage and

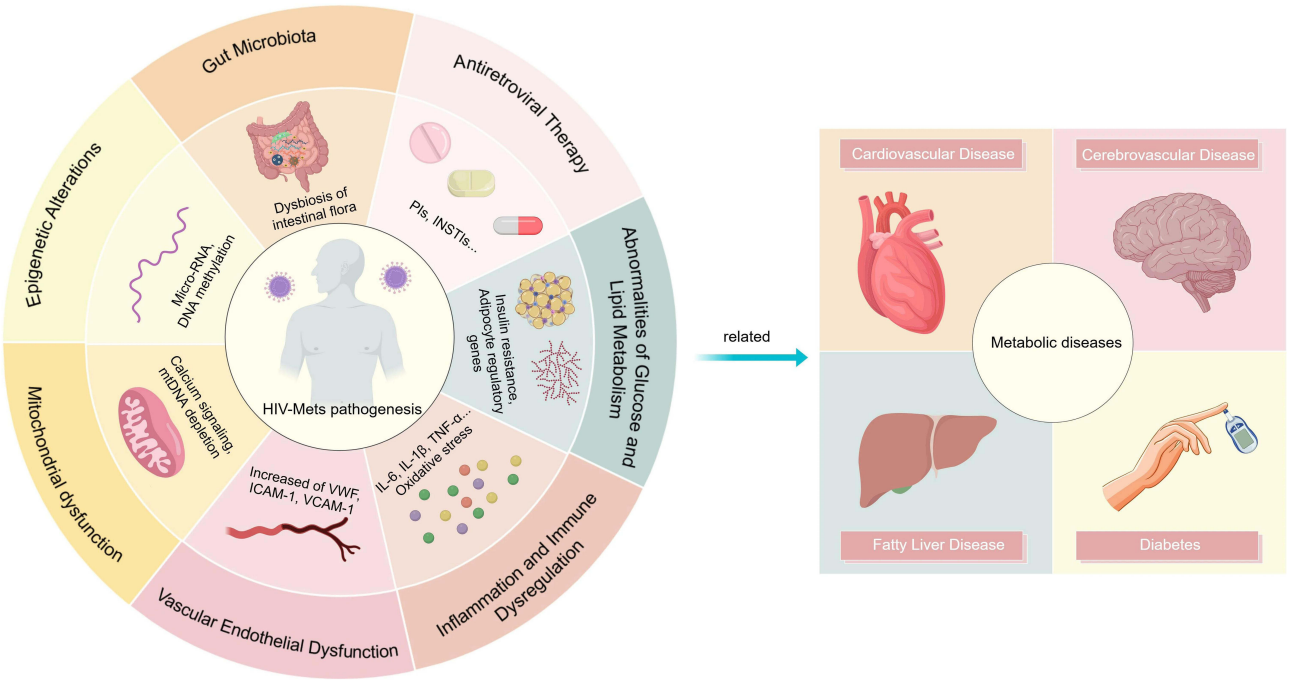

Figure 1 Potential mechanisms of HIV-MetS, and the increased likelihood of metabolic diseases such as T2DM, NAFLD, cardiovascular and cerebrovascular diseases following HIV infection.

Table 2 Mechanistic Hypotheses of HIV-Associated Metabolic Syndrome

Hypothesis Name	Core Concept	Main Mechanisms
Drug Side Effects Hypothesis	Different ART drugs have variations in metabolic effects; PIs and NRTIs can directly cause metabolic abnormalities, markedly increasing MetS risk.	• Impairment of fat cell differentiation • Mitochondrial dysfunction • Systemic inflammation and adipokine dysregulation • Insulin resistance • Epigenetic modifications abnormalities
Chronic Inflammation and Immune Activation Hypothesis	HIV infection and ART induce chronic inflammation and immune activation, promoting metabolic disorders (such as insulin resistance, dyslipidemia).	• Abnormal activation of immune cells (exhaustion and dysregulation of CD4+ T cells, hyperactivation of monocytes/macrophages) • Chronic inflammatory microenvironment (elevated inflammatory markers, adipose tissue inflammation) • Synergistic effects of antiretroviral drugs • Abnormalities in immune gene epigenetics Endothelial damage and dysfunction
Insulin Resistance Hypothesis	HIV infection and ART induce insulin resistance, leading to MetS.	• Insulin signaling disorder • Decreased insulin sensitivity and hyperinsulinemia • Increased free fatty acid (FFA) release • Fat factor imbalance and inflammation • Vicious circle of metabolic disorders
Mitochondrial Dysfunction Hypothesis	HIV infection and ART cause mitochondrial dysfunction, abnormal energy metabolism, leading to characteristic features of MetS.	• NRTIs directly inhibits mitochondrial DNA synthesis • Respiratory chain energy metabolism disorder • Dysregulation of calcium homeostasis • Oxidative stress and inflammation • Abnormal morphology and function of adipocytes
Immune-Lipid Interaction Hypothesis	HIV activates the immune system, impacting lipid metabolism.	• Immune-mediated adipose tissue injury • Drugs directly interfere with metabolic pathways • Adipose tissue dysfunction and abnormal lipid metabolism • Fat redistribution and metabolic complications
Epigenetic Modifications Hypothesis	HIV infection and ART alter host cell epigenetic regulation, leading to chronic inflammation, immune dysregulation, and metabolic abnormalities.	• Abnormal DNA methylation; • Histone modification dysregulation; • Immune and cellular aging.
Gut Microbiota Dysbiosis Hypothesis	HIV infection leads to gut microbiota imbalance, promoting chronic immune activation, microbial translocation, and systemic inflammation, which drive metabolic abnormalities.	• Dysbiosis and immune activation; • Reduction of anti-inflammatory bacteria; • Tryptophan metabolism abnormalities; • Intestinal barrier damage and microbial translocation; • Impairment of AhR signaling pathway.

dysfunction, contributing to the development of hypertension, coronary heart disease, and other cardiometabolic pathologies.[93] Certainly, persistent systemic inflammation also exacerbates immunosenescence (eg, telomere shortening in T cells and expansion of senescent phenotypes), accelerating biological aging processes.[94,95] This significantly increases the risk of MetS and advances its onset.[96]

Mitochondrial Dysfunction

Mitochondria play a pivotal role in energy metabolism and oxidative stress while also being a critical link in HIV-induced inflammatory states and cellular immune dysregulation. A report reveals that specific mitochondrial haplogroups exhibit significant associations with the development of MetS in PLWH, suggesting that mitochondrial genetic

backgrounds may play a critical role in this population.[97] Mitochondrial dysfunction can lead to disruptions in energy metabolism, subsequently triggering characteristic manifestations of MetS, such as insulin resistance, obesity, and hypertension. Specifically, HIV infection induces mitochondrial dysfunction—including mitochondria-mediated apoptosis, mitochondrial DNA (mtDNA) depletion, impaired calcium signaling, and mitochondrial membrane dysfunction. These alterations impair fatty acid oxidation and energy production, thereby driving metabolic abnormalities.[38] The mechanisms involve HIV-related activation of inflammatory pathways, oxidative stress from excessive reactive oxygen species (ROS), and direct mitochondrial toxicity from antiretroviral drugs (eg, nucleoside reverse transcriptase inhibitors like zidovudine), which inhibit mitochondrial DNA polymerase γ and reduce mtDNA synthesis.[98–100] This cascade of mitochondrial damage amplifies systemic inflammation and perpetuates metabolic dysregulation through lipid accumulation, insulin signaling defects, and impaired cellular homeostasis.[101]

Vascular Endothelial Dysfunction

The activation, injury, and dysfunction of vascular endothelium have been extensively documented in HIV-MetS, representing a pivotal mechanism through which chronic inflammation contributes to the development of MetS.[102] PLWH exhibits elevated levels of endothelial activation markers such as von Willebrand factor (vWF), intercellular adhesion molecule-1 (ICAM-1), and vascular cell adhesion molecule-1 (VCAM-1).[103–106] Although ART can reduce these marker levels, they remain significantly higher than those observed in the general population.[107] A study of untreated PLWH reported that HIV infection is associated with impaired arterial elasticity in both large and small vascular systems.[108] Evidence indicates that PLWH exhibits significantly increased arterial stiffness, which is associated with impaired cerebrovascular reactivity, heightened immune activation, elevated inflammatory markers, and accelerated cellular senescence. Severe endothelial dysfunction may further correlate with increased microvascular oxidative stress and reduced levels of nitric oxide (NO) and arginine. These alterations collectively destabilize circulatory homeostasis and elevate the risk of MetS.[102,109–111]

Abnormalities of Glucose and Lipid Metabolism

The lipid metabolism abnormalities caused by HIV have been extensively studied. Most PLWH develop lipodystrophy, primarily characterized by central lipohypertrophy with increased visceral fat deposition and peripheral lipoatrophy (limb fat reduction).[112] Lipidomic studies have revealed that the most common lipid abnormalities in PLWH include hypertriglyceridemia, low high-density lipoprotein cholesterol (HDL-C) levels, and elevated low-density lipoprotein cholesterol (LDL-C) and total cholesterol levels.[113]

HIV infection can also lead to glucose metabolism disorders,[114] although the specific mechanisms remain unclear. Current research suggests that most PLWH exhibit insulin resistance(IR). Compared to uninfected individuals, PLWH demonstrate elevated glucose uptake rates and increased levels of glycolytic intermediates.[115]

The mechanism may involve dysregulated expression of adipocyte regulatory genes, aberrant secretion of various cytokines, and subsequent disruptions in adipocyte maturation, lipid distribution, and glucose metabolism pathways.[19,112] Specifically, after infecting the human body, HIV can persist long-term in adipose tissue reservoirs, continuously releasing viral proteins such as Nef protein, glycoprotein 120 (gp120), and the HIV accessory protein Vpr.[92] These transcriptional disturbances cause abnormal adipocyte differentiation and dysfunction, simultaneously increasing free fatty acids' transport to skeletal muscle and liver.[116,117] Concurrently, HIV infection triggers the production of antiviral-related cytokines like IFN-α and IL-6. These cytokines may contribute to elevated serum triglycerides by interfering with lipid clearance processes.[118] For instance, Nef protein and gp120 can upregulate cytokine levels, including IL-6, IL-1βand TNF-α.[119] These changes disrupt insulin signaling by affecting the insulin receptor substrate 1 (IRS-1) and phosphoinositide 3-kinase (PI3K) pathway, thereby inducing IR. These alterations further promote hepatic gluconeogenesis and stimulate triglyceride secretion from the liver. Meanwhile, elevated TNF-α exacerbates insulin resistance through dual mechanisms: by reducing insulin receptor kinase activity and downregulating IRS-1 and glucose transporter 4 (GLUT4), which subsequently induces adipocyte apoptosis and lipolysis.[120] IR impairs the inhibitory effect of insulin on lipolysis, leading to increased release of FFA. Elevated FFA are taken up by peripheral tissues, interfering with insulin signaling and exacerbating IR; simultaneously, they promote hepatic gluconeogenesis and triglyceride synthesis,

resulting in hyperglycemia and dyslipidemia.[121,122] They also promote vascular endothelial dysfunction and increased renal sodium reabsorption, contributing to the development of hypertension and coronary heart disease.[123]

Gut Microbiota

The microbiota has been recognized as a pivotal player capable of tipping the balance between health and disease. The human gut constitutes a nutrient-rich environment colonized by a vast array of microbial species, collectively referred to as the "gut microbiota" (GM). The gut microbiota is closely associated with numerous diseases, including metabolic syndrome, AIDS, and obesity.[124,125]

An increasing number of scholars believe that the occurrence of HIV-MetS is closely linked to abnormalities in gut microbiota. Specific mechanisms may involve the following aspects:

Impairment of the Intestinal Barrier and Microbial Translocation

HIV (particularly its gp120 envelope glycoprotein) downregulates tight junction proteins (such as claudin, occludin, and ZO-1), and increases intestinal permeability. This leads to the translocation of microbes and their products into the systemic circulation,[126,127] resulting in metabolic endotoxemia. For instance, lipopolysaccharide (LPS) from Gram-negative bacteria enters the bloodstream and triggers systemic inflammation via activation of the TLR/CD14 pathway, promoting IR and dyslipidemia.[128–130] Furthermore, LPS activates the coagulation cascade and increases the production of procoagulant tissue factors, thereby impacting metabolism.[95] Moreover, during the early stages of infection, HIV preferentially destroys CCR5+ CD4+ T cells in the gut-associated lymphoid tissue (GALT), exacerbating CD4+ T cell depletion, weakening mucosal immune defenses, and further promoting the loss of barrier function.[131] Even early initiation of antiretroviral therapy may not fully prevent gut microbiota dysbiosis or bacterial translocation.[127]

Dysbiosis and Immune Activation

Studies have found that in HIV-infected individuals, there is an enrichment of pathogenic bacteria such as Proteobacteria in the gut, while commensal bacteria such as Bacteroidetes are reduced.[126,127,132] The dysbiotic microbiota directly activates gut immune cells, leading to T-cell activation and the release of pro-inflammatory cytokines (such as IL-6 and TNF-α), triggering chronic inflammation. Moreover, dysbiotic microbiota can lead to a deficiency in short-chain fatty acids (SCFAs), affecting metabolic homeostasis.[133] SCFAs deficiency is associated with chronic inflammation and increased morbidity/mortality.[133]

Abnormal Tryptophan Metabolism

Dysbiotic microbiota enhances tryptophan catabolism, activating the kynurenine pathway. This process depletes tryptophan and generates neurotoxic metabolites, further exacerbating inflammatory responses and T-cell dysfunction, and is positively correlated with disease progression markers such as elevated IL-6.[132]

Impaired AhR Signaling Pathway

Reduced production of aryl hydrocarbon receptor (AhR) ligands by a dysbiotic microbiota impairs gut barrier repair, attenuates IL-22 signaling (affecting mucosal immunity), and decreases GLP-1 secretion (affecting glycemia regulation), collectively exacerbating metabolic disorders.[95,130]

Reduction in Anti-Inflammatory Microbiota

In HIV-MetS patients, anti-inflammatory gut bacteria such as Alistipes are significantly reduced, impairing the microbiota's negative regulatory role in inflammation and further amplifying inflammation associated with metabolic abnormalities. The depletion of Alistipes can be considered a core feature of gut dysbiosis in HIV-MetS patients, leading to elevated inflammatory markers of metabolic syndrome and increased cardiovascular risk.[134,135]

Epigenetic Alterations

In addition to the aforementioned mechanisms, epigenetic alterations have also been implicated in recent research. Specifically, HIV infection can induce aberrant global DNA methylation levels in host cells, characterized by downregulation of DNA methyltransferase (DNMT) and upregulation of methyl-CpG-binding proteins (such as MBD2).[136]

This increases monocyte activation status and the production of pro-inflammatory cytokines (eg, TNF-α, IL-6),[91] thereby exacerbating insulin resistance and lipid metabolism disorders. For instance, HIV infection induces DNA methylation changes in essential genes (eg, IL-2, PD-1, and FOXP3) within T cells, triggering monocyte dysfunction and enhanced pro-inflammatory cytokine production.[38,137] During HIV latent infection, histone modifications in the viral promoter region (such as increased H3K9me3 methylation and reduced H3 acetylation) suppress viral gene transcription, establishing the latent reservoir.[138] Concurrently, aberrant histone modifications (eg, acetylation imbalance) in host inflammation-related genes further sustain chronic inflammation and promote metabolic complications.

In the ART population, alterations in epigenetic modifications are associated with changes in micro-RNA expression. Studies have shown that ART drugs can reduce the expression of miR-140 and miR-106a and increase the levels of miR-192. This, in synergy with HIV, exacerbates abnormalities in epigenetic modifications, amplifies inflammatory responses and mitochondrial dysfunction, promotes immune activation,[34] immune senescence,[136] and drives the development of MetS.

Therefore, the epigenetic alterations induced by HIV or ART ultimately require synergy with inflammation, immune dysregulation, metabolic disturbances, and mitochondrial dysfunction to collectively promote the development of HIV-associated metabolic syndrome (HIV-MetS). The precise mechanisms underlying this process require further investigation.

Antiretroviral Therapy

Numerous studies have demonstrated that PLWH receiving ART exhibits a higher incidence of MetS compared to untreated PLWH. A prospective analysis revealed that the prevalence of MetS among PLWH increased by 8.4% after 48 weeks of ART.[139] Current perspectives suggest that both HIV infection and long-term ART collectively elevate the risk of MetS,[140] with the role of ART medications receiving increasing attention. Antiretroviral drugs for HIV/AIDS are diverse, including protease inhibitors (PIs), non-nucleoside reverse transcriptase inhibitors (NNRTIs), nucleoside reverse transcriptase inhibitors (NRTIs), integrase strand transfer inhibitors (INSTIs), HIV entry inhibitors, and fusion Inhibitors (FIs).

The differential effects of various antiretroviral drugs on the metabolic profile of PLWH have been controversial, while research on lipid metabolism is relatively well-established (Table 3). HIV entry inhibitors exert minimal impact on lipid profiles, while other antiretroviral drugs may potentially induce dyslipidemia. PIs and NRTIs demonstrate the most pronounced metabolic toxicities,[141,142] primarily involving mitochondrial dysfunction, suppression of lipid synthesis pathways, and interference with insulin signaling. INSTIs are associated with weight gain and hypertriglyceridemia. NNRTIs typically induce milder dyslipidemia.

The specific mechanisms are detailed below:

Table 3 The Impact of Different ART Drugs on Blood Lipids

Category	Specific Drugs	Effects on Blood Lipids
PIs	RTV, ATV, DRV, etc.	↑↑ TG, ↑↑ LDL, ↑↑ HDL
NRTIs	TDF	Normal or decreased TG and TC; phosphate abnormalities, fat distribution abnormalities
	ZDV	↑ TG and ↑ LDL; lactic acidosis, fat degeneration/atrophy
	TAF	↑ TG, ↑ LDL, ↑ HDL; weight gain
INSTIs	EVG	↑ TG, ↑ LDL, ↑ HDL
NNRTIs	EFV, NVP	↑↑ TG, ↑↑ LDL, ↑↑ HDL; male breast development
	ETV, RPV	Minimal effects
HIV Entry Inhibitors	MVC, ENF	Essentially no effect

Abbreviations: RTV, Lopinavir; ATV, Atazanavir; DRV, Darunavir; TDF, Tenofovir Disoproxil fumarate; ZDV, Zidovudine; TAF, Tenofovir Alafenamide; EVG, Elvitegravir; EFV, Efavirenz; NVP, Nevirapine; ETV, Etravirine; RPV, Rilpivirine; MVC, Maraviroc; ENF, Enfuvirtide; TG, Triglycerides; LDL, Low-Density Lipoprotein; HDL, High-Density Lipoprotein.

PIs

Almost all protease inhibitors (PIs) can cause metabolic abnormalities, while atazanavir is among the PIs with relatively minor effects on lipids. The specific mechanism is as follows:[143–150]

① Inhibition of mitochondrial DNA polymerase, causing oxidative stress and mitochondrial dysfunction and leading to respiratory chain dysfunction, insulin resistance, and lipodystrophy.

② Suppression of the degradation of sterol regulatory element-binding protein-1 (SREBP-1) in adipose tissue and the liver, resulting in dyslipidemia and hepatic steatosis.

③ ER stress induced by PIs activates the unfolded protein response (UPR), which enhances hepatic lipid synthesis and inflammatory cytokine release, aggravating metabolic disorders.

④ Inhibition of cellular retinoic acid-binding protein-1 (CRABP-1), which reduces peroxisome proliferator-activated receptor gamma (PPAR-γ) activity. This leads to increased adipocyte apoptosis, impaired adipocyte maturation, and lipodystrophy.

⑤ Impairment of glucose transporter GLUT4 induces IR.

⑥ Reduction in adiponectin levels suppresses lipoprotein lipase on capillary endothelium, elevating triglyceride and insulin concentrations, thereby promoting adipose tissue dysfunction.

NRTIs

NRTIs can cause hyperlactatemia, abnormal fat distribution, and hypophosphatemia. The proposed mechanisms are:[38,150] ① Inhibition of mitochondrial DNA polymerase gamma, leading to mitochondrial dysfunction and subsequent lactic acidosis, hepatic steatosis, and insulin resistance; ② Direct interference with adipocyte differentiation by certain drugs (such as stavudine (d4T) and zidovudine (ZDV)), resulting in lipoatrophy.

INSTIs

Some INSTIs (eg, Elvitegravir) may cause weight gain and hypertriglyceridemia. The mechanism is likely associated with epigenetic modifications (such as DNA methylation) affecting metabolic gene expression and disrupting energy balance regulation,[38] though further investigation is needed.

NNRTIs

The impact of NNRTIs on blood lipids is relatively mild. For instance, efavirenz (EFV) can mildly induce CYP450 enzymes, indirectly affecting lipid metabolism, whereas nevirapine (NVP) can cause abnormalities in HDL and LDL,[148] and its mechanism requires further investigation.

The exact mechanisms by which ART induces MetS have not yet been fully elucidated. Current evidence suggests potential associations with post-ART alterations in hepatic synthetic function, inflammatory responses, oxidative stress, and genetic factors.[113] Additionally, the pathogenesis involves multiple interrelated mechanisms, including abnormal secretion of adipokines, lipodystrophy, insulin resistance, impaired glucose metabolism, and endothelial dysfunction.

Management Recommendations

Diagnostic Criteria

Current diagnostic criteria for HIV-MetS primarily reference internationally recognized definitions, varying across countries and ethnicities.[12] Commonly used standards include:

NCEP/ATP III criteria (National Cholesterol Education Program Adult Treatment Panel III, 2001),[13] IDF criteria (International Diabetes Federation, 2005),[15] Harmonized criteria (IDF/AHA/NHLBI consensus,2009),[12] DS criteria (Chinese Diabetes Society, 2004/2013)[151] and so on. Detailed components of these criteria are summarized in Table 1.

In clinical practice, it is recommended to integrate HIV-specific factors (eg, ART types) with general criteria and adjust waist circumference cutoff points based on population characteristics (eg, ethnicity, age, gender). Future efforts should focus on standardizing HIV-MetS diagnostic criteria to enhance comparability across studies.

Risk Factors and Risk Assessment

The risk factors for HIV-MetS encompass HIV-related factors (eg, HIV infection, CD4 T-cell count, ART) and traditional factors (eg, genetic predisposition, gender, age, high-fat/high-sugar diets, smoking, alcohol consumption, insulin resistance, obesity, physical inactivity).[152]

Due to the heightened MetS among PLWH, CVD risk assessment is imperative for this population. However, there is currently no specific risk assessment model tailored for MetS in PLWH. In 2020, the Infectious Diseases Society of America (IDSA) emphasized for the first time that cardiovascular risk assessment should be universally conducted for elderly PLWH. Their guidelines recommend the use of the 2013 American College of Cardiology/American Heart Association (ACC/AHA) Pooled Cohort Equations. Studies have also proposed alternative scoring systems, such as the D:A:D model and VACS score. However, these existing systems may underestimate the cardiovascular risk in PLWH,[153] underscoring the urgent need to develop updated and more comprehensive risk assessment frameworks.[154]

Health Education and Lifestyle Intervention

Health education serves as a crucial foundation for the prevention and treatment of HIV-MetS, with lifestyle interventions forming the cornerstone of management. Diversified and accessible educational approaches—utilizing manuals, instructional videos, and digital media platforms—can effectively raise awareness about metabolic syndrome and encourage early adoption of healthy lifestyle modifications.[155] Lifestyle intervention refers to the management of modifiable risk factors, as detailed below:

1. Smoking Cessation: Research indicates that PLWH exhibit a significantly higher prevalence of smoking compared to the general population[156–159] Smoking cessation has been shown to improve life expectancy among middle-aged and elderly PLWH[160] Therefore, it is strongly recommended that HIV-MetS abstain from smoking to mitigate health risks.
2. Limiting alcohol intake: Excessive alcohol consumption is commonly associated with HIV transmission and disease progression.[161] Alcohol abuse has clear detrimental effects on PLWH, potentially increasing the risk of metabolic disorders, and it is strongly recommended that PLWH restrict alcohol consumption.[162–164] However, the specific safe threshold for alcohol intake among HIV-MetS remains to be further investigated.
3. Dietary: Dietary intervention serves as an early and effective strategy against MetS [125] and can precede pharmacological treatment.[165] Multiple studies on nutritional counseling and management in PLWH have demonstrated that dietary modifications significantly improve body mass index (BMI), lipid profiles,[166–169] and reduce cardiovascular disease risk.[170] Various dietary patterns are recommended for MetS management, including the Mediterranean diet, New Nordic diet, DASH (Dietary Approaches to Stop Hypertension) diet, and the Chinese Balanced Dietary Pattern for Residents.[7,171,172] For PLWH with MetS, adherence to these patterns is advised, emphasizing adequate energy intake, sufficient protein, vitamins, and minerals, while prioritizing low refined sugars, low-carbohydrate, low-cholesterol, and low-sodium diets .[168] However, due to variations in metabolic demands and nutritional status among PLWH, individualized dietary planning remains crucial.
4. Physical exercise and weight management: Considering individual factors such as age and cardiopulmonary capacity, select appropriate exercise types and adjust intensity. Moderate-intensity physical activity is generally recommended, with a focus on aerobic exercises, work-related activities, and muscle-strengthening training, while regularly monitoring BMI.[173] Overweight individuals are advised to regularly (every 3–6 months) assess organ function, endocrine status, and mental health during exercise to effectively manage weight-related complications.[174]

Lipid Management

Lipid management is crucial in the management of both general MetS patients and PLWH. The American College of Cardiology/American Heart Association/Multi-Society (ACC/AHA/MS) guidelines identify HIV as a potential risk-enhancing factor for cardiovascular events.[175] Recent studies on HIV-associated cardiovascular events have shown that daily administration of 4 mg pitavastatin reduced cardiovascular events by 35% in PLWH compared to the control.[176]

However, statins may also increase the incidence of diabetes and muscular adverse events.[177–179] The current mainstream consensus holds that statins are the foundation for lipid-lowering and cardiovascular risk reduction in PLWH with dyslipidemia.[180] It is recommended that all PLWH at high 10-year ASCVD risk (assessed using the 2013 ACC/AHA Pooled Cohort Equations) receive statin therapy, while treatment decisions for intermediate- to low-risk individuals should be made on a case-by-case basis, considering clinical contexts.

In the selection of lipid-lowering medications, decisions should be based on varying cardiovascular risks and the concurrent use of different antiviral drugs.[181]

The American College of Cardiology and the HIV Medicine Association recommend the following[182](specific drug options in Table 4):

• For HIV-infected individuals aged <40 years with low-to-moderate 10-year ASCVD risk (<20%), lifestyle modifications are prioritized for lipid control.

• For PLWH (People Living with HIV) aged 40–75 years with an estimated 10-year ASCVD risk of 5%–20% or diabetes alone, moderate-intensity statins are recommended.

• For high-risk groups (≥20% 10-year ASCVD risk for those aged 40–75, or LDL-C ≥190 mg/dL for individuals aged 20–75), high-intensity statins should be initiated.

• Other cases should be determined based on specific clinical circumstances.

Regarding the combined use with ART medications, generally, pitavastatin, low-dose atorvastatin, and rosuvastatin have a lower likelihood of interacting with ART and can be safely used. In contrast, ezetimibe, PCSK9 inhibitors, fibrates, and some newer drugs may pose certain risks and require cautious selection.[113]

Other lipid-lowering agents, such as ezetimibe, PCSK9 inhibitors, high-purity fish oil (eg, icosapent ethyl), bempedoic acid, and small interfering RNA (siRNA) had been reported in hyperlipidemic patients.[179,183] However, their specific usage data and indications still require further validation.

Blood Glucose Management

There is currently no unified guideline for blood glucose management in patients with HIV-associated metabolic syndrome. Most studies recommend that persons living with HIV (PLWH) undergo annual diabetes screening, with regular monitoring of blood glucose and glycemic markers (eg, HbA1c) based on specific national guidelines.[64] For PLWH who do not meet the diagnostic criteria for diabetes, blood glucose management can be achieved through lifestyle interventions alone.[184] For those who meet the diagnostic criteria, a metformin-based pharmacotherapy regimen is required, with insulin therapy introduced as needed to achieve glycemic control.[185,186]

Blood Pressure Management

National Institutes of Health (NIH) recommends continuous blood pressure monitoring for PLWH, including those with MetS. Similar to blood glucose management, there are currently no established mandatory standards for blood pressure management in HIV- MetS patients. However, the blood pressure targets for HIV-only patients (<140/90 mmHg or <130/80 mmHg) remain consistent with those for non-HIV individuals[187] and should be tailored based on individual risk profiles.

Table 4 Classification of Statin Therapy Intensity

	Low Intensity	Moderate Intensity	High Intensity
Recommended Medications	Pravastatin 10–20mg/d Simvastatin 20–40mg/d Lovastatin 20mg/d Fluvastatin 20mg/d	Pitavastatin 4mg/d Atorvastatin 20mg/d Rosuvastatin 10mg/d	Atorvastatin 40–80mg/d Rosuvastatin 20–40mg/d
Treatment Goal (LDL-C Reduction Percentage)	<30%	30%–49%	≥50%

Antiretroviral Drug

The selection of antiretroviral drug regimens requires careful consideration, as different classes of drugs exert distinct metabolic effects (Table 3). Current international guidelines primarily recommend first-line ART regimens based on INSTI-based triple therapy.[188] Commonly used INSTIs, such as dolutegravir, raltegravir, and elvitegravir, effectively suppress viral load. However, they may significantly affect lipid metabolism, leading to notable weight gain and increasing the risk of metabolic syndrome in PLWH. Therefore, when selecting an ART regimen, it is essential to balance efficacy, adverse effects, patient adherence, and potential metabolic comorbidities. Newer agents, such as long-acting intramuscular INSTIs (eg, cabotegravir) and HIV entry inhibitors (including CCR5 antagonists, attachment inhibitors, and fusion inhibitors), offer promising alternatives due to their minimal adverse effects on metabolic parameters .[113]

Inequality of Medical Resources

The development of HIV-MetS is linked to multiple factors, including income disparities and inequitable distribution of healthcare resources. In underrepresented regions (such as many low- and middle-income countries), the scarcity of medical resources significantly constrains the diagnosis and management of HIV-MetS. This not only exacerbates the disease burden for affected individuals but also impedes the achievement of public health objectives.

Sub-Saharan African countries (eg, Ghana, Nigeria, Cameroon) bear nearly two-thirds of the global burden of HIV infection. However, due to weak healthcare infrastructure, limited laboratory resources, and shortages of specialized medical personnel, metabolic abnormalities among PLWH are often unrecognized. This leads to missed opportunities for early intervention, increases comorbidity management challenges, and ultimately results in significantly higher non-HIV-related mortality rates in this region compared to developed countries or regions.[2,189,190] In Latin America (eg, Brazil, Peru) and parts of South America (eg, Colombia, Argentina), the prevalence of HIV-MetS varies substantially, ranging from 8% to 52%.[191,192] Similarly, in resource-limited Asian regions (eg, Cambodia, Laos, Vietnam, India), the prevalence is approximately 10% to 42%.[21,193] This reflects regional disparities in healthcare resource allocation, particularly in remote areas, where limited access to antiviral drugs, insufficient specialist coverage, and inadequate primary care resources increase the difficulty of identifying and managing HIV-MetS, thereby compromising CVD risk control in patients.[194] Additionally, inequalities faced by transgender populations are highlighted. A US study indicates that transgender women living with HIV encounter greater barriers to viral suppression and health management compared to cisgender individuals with HIV, underscoring the compounded disadvantages in resource access among marginalized groups.[195]

Scholars have advocated for international collaboration, technological innovation, and policy support to optimize resource allocation regionally, promote equitable treatment access, and enhance the overall quality of life and health outcomes for HIV-MetS patients. Specific measures include introducing low-cost screening tools, strengthening training for primary healthcare workers, optimizing medication supply and utilization, promoting health education, and establishing sustainable monitoring systems in resource-limited settings.

Others

Measures for the prevention, diagnosis, and treatment of HIV-MetS are under ongoing investigation.

For diagnostic evaluation, studies propose using estimated pulse wave velocity (ePWV) as a novel non-invasive biomarker for MetS in PLWH ,[189] while machine learning-based retinal image analysis has shown a potential to improve the accuracy of CAD risk in this population.[190,191]

For prevention and treatment, probiotics have emerged as a potential therapeutic target for non-AIDS comorbidities like metabolic disorders and CAD,[192] though interventions such as probiotic supplementation, prebiotics, and fecal microbiota transplantation require further validation of efficacy.[193] Traditional Chinese medicine (TCM) may correct "lipid metabolism imbalance" and restore systemic homeostasis, offering a therapeutic approach for HAART-induced hyperlipidemia.[194,195] Other modalities, including plant-based antioxidant therapies, await further development .[171]

For management, advocate for establishing a patient-centered, stigma-free specialized healthcare environment, creating a research-oriented big data platform, and implementing a "one-stop service" model that integrates real-time follow-up management for HIV/AIDS patients and multidisciplinary team support comprising infectious disease specialists, nutritionists,

metabolic disease experts, pharmacists, and social workers to deliver comprehensive, refined, and individualized patient care throughout the entire treatment process[155].

Conclusions and Future Perspectives

Research over recent decades has demonstrated that PLWH exhibit a higher incidence of MetS compared to the general population. HIV-MetS also elevates the risk of complications including cardiovascular disease, diabetes, fatty liver disease, stroke, dementia, and premature aging, significantly compromising patients' quality of life and survival rates. Consequently, early identification, intervention, and standardized management for this population are critically important.

The pathogenesis of HIV-MetS is complex, primarily centered on the HIV virus itself and ART. It involves chronic inflammation and immune activation, glucose and lipid metabolism abnormalities, mitochondrial dysfunction, vascular endothelial abnormalities, gut microbiota dysbiosis, epigenetic alterations, and the use of specific ART drugs. These mechanistic insights provide potential avenues for developing novel therapeutic drugs for HIV-MetS. Research into these mechanisms, however, should not stop at this point, as significant gaps remain that require in-depth, systematic, and detailed exploration.

HIV-MetS involves numerous contributing factors, making clinical management and treatment notoriously challenging. In recent years, personalized integrated management strategies aimed at improving the long-term prognosis of PLWH have emerged. These include optimizing ART regimens, implementing lifestyle interventions (such as smoking cessation, alcohol restriction, dietary control, exercise, and weight management), and managing glycemia, blood pressure, and dyslipidemia. Among these, lipid management and treatment are of paramount importance. Additionally, risk assessment utilizing inflammatory markers and genetic factors, establishment of a multidisciplinary integrated care model, application of probiotics or gut barrier restoratives, and stratification of patients based on metabolomic/microbiome profiles were also addressed in this article.

Certainly, significant research gaps remain to be addressed. Current limitations include insufficient longitudinal data, ethnic and regional epidemiological variations, regional disparities in healthcare resource allocation, and inadequate research data on HIV-MetS in children. Equally lacking are effective HIV-MetS risk assessment models, large-scale clinical trials for MetS prevention and management in PLWH, and evidence-based MetS guidelines tailored for specific PLWH populations (such as the elderly, children, and women).

Future research directions on HIV-MetS may include developing novel antiretroviral drugs with reduced metabolic impact, exploring antioxidant and anti-inflammatory targeted therapies, investigating gut microbiota modulation approaches, and developing immunomodulatory agents (eg, cytokines and small-molecule drugs) as well as therapeutics targeting metabolic signaling pathways. Additionally, low-cost metabolic screening models should be promoted in aging PLWH. Crucially, future research should not only focus on mechanistic studies, risk model development, and pharmacological interventions but also consider establishing metabolic specialty clinics in resource-limited settings (eg, Africa) to enhance cardiovascular risk assessment; promote gender-, age-, and ethnicity-specific management guidelines; integrate comprehensive care models encompassing assessment, treatment, nursing, follow-up, and psychological support; and strengthen global public health strategies targeting prevention and intervention in low-resource environments.

This comprehensive review synthesizes the pathogenesis, diagnostic criteria, risk factors, and clinical management strategies of HIV-MetS. These findings directly provide a foundation for developing evidence-based risk models for HIV-MetS, and inform WHO guidelines for HIV care and national HIV management protocols, particularly in aging populations with comorbid metabolic disorders. It is hoped that in the near future, individualized management for the HIV-MetS population will reduce global health inequities, alleviate the growing burden of HIV-related diseases and economic costs, and advance comprehensive health equity.

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Author Contributions

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reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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References

1. UNAIDS. Global HIV & AIDS statistic: Fact sheet; 2025. Available from: https://www. unaids. org/en/ resources/fact-sheet.
2. Hiv TL. UNAIDS strategy aligns HIV priorities with development goals. *Lancet HIV*. 2021;8(5). doi:10.1016/S2352-3018(21)00278-2
3. S ASV, S D, KK L, et al. Global Burden of Atherosclerotic Cardiovascular Disease in People Living With HIV: systematic Review and Meta-Analysis. *Circulation*. 2018;138(11):1100–1112. doi:10.1161/CIRCULATIONAHA.117.033369
4. Odikro MA, Torpey K, Lartey M, Puplampu P, Painstil E. Incidence, risk factors for metabolic syndrome and health systems capacity for its management amongst people living with HIV, Accra-Ghana: a study protocol. *PLoS One*. 2024;19(11):e0312446. doi:10.1371/journal.pone.0312446
5. Nguyen KA, Peer N, Mills EJ, Kengne AP, Menéndez-Arias L. A Meta-Analysis of the Metabolic Syndrome Prevalence in the Global HIV-Infected Population. *PLoS One*. 2016;11(3):e0150970. doi:10.1371/journal.pone.0150970
6. Schouten J, Wit FW, Stolte IG, et al. Cross-sectional comparison of the prevalence of age-associated comorbidities and their risk factors between HIV-infected and uninfected individuals: the AGEhIV cohort study. *Clin Infect Dis*. 2014;59(12):1787–1797. doi:10.1093/cid/ciu701
7. Fahed G, Aoun L, Bou Zerdan M, et al. Metabolic Syndrome: updates on Pathophysiology and Management in 2021. *Int J Mol Sci*. 2022;23 (2):786. doi:10.3390/ijms23020786
8. Gami A, Witt B, Howard D, et al. Metabolic syndrome and risk of incident cardiovascular events and death: a systematic review and meta-analysis of longitudinal studies. *Journal of the American College of Cardiology*. 2007;49(4):403–414. doi:10.1016/j.jacc.2006.09.032
9. Kalligeros MVA, Shehadeh F, Vassilopoulos S, et al. Prevalence and Characteristics of Nonalcoholic Fatty Liver Disease and Fibrosis in People Living With HIV Monoinfection: a Systematic Review and Meta-analysis. *Clinical Gastroenterology and Hepatology: the Official Clinical Practice Journal of the America*. 2023;21(7):1708–1722. doi:10.1016/j.cgh.2023.01.001
10. So-Armah KBL, Benjamin LA, Bloomfield GS. Bloomfield GS,Feinstein MJ,Hsue P,Njuguna B,Freiberg MS. HIV and cardiovascular disease. *The Lancet HIV*. 2020;7(4):e279–e93. doi:10.1016/S2352-3018(20)30036-9
11. Tang J, Chen L, Pan W, et al. Prevalence of metabolic syndrome in people living with HIV and its multi-organ damage: a prospective cohort study. *BMC Infect Dis*. 2025;25(1):351. doi:10.1186/s12879-025-10735-7
12. Alberti KG, Eckel RH, Grundy SM, et al. Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. *Circulation*. 2009;120(16):1640–1645. doi:10.1161/CIRCULATIONAHA.109.192644
13. Grundy SM, Cleeman JI, Daniels SR, et al. Diagnosis and management of the metabolic syndrome: an American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement. *Circulation*. 2005;112(17):2735–2752. doi:10.1161/CIRCULATIONAHA.105.169404
14. Grundy SM, Cleeman JI, Daniels SR, et al. Diagnosis and management of the metabolic syndrome: an American Heart Association/National Heart, Lung, and Blood Institute scientific statement. *Curr Opin Cardiol*. 2006;21(1):1–6. doi:10.1097/01.hco.0000200416.65370.a0
15. Alberti KG, Zimmet P, Shaw J. Metabolic syndrome--a new world-wide definition. A Consensus Statement from the International Diabetes Federation. *Diabet Med*. 2006;23(5):469–480. doi:10.1111/j.1464-5491.2006.01858.x
16. M R-P, G A, R P, Ł M, F R. Metabolic syndrome in HIV infected adults in Poland. *Kardiologia polska*. 2018;76(3):548–553. doi:10.5603/KP.a2017.0249
17. Edith P, Carla MTF, Aletta ES. The metabolic syndrome and renal function in an African cohort infected with human immunodeficiency virus. *South Afr J HIV Med*. 2018;19(1):1.
18. Titus FM, Gary PVG, Yvo MS, Marceline VF, John AB, Michiel AVA. Association of HIV-infection, antiretroviral treatment and metabolic syndrome with large artery stiffness: a cross-sectional study. *BMC Infect Dis*. 2018;18(1):2.
19. Masenga SK, Elijovich F, Koethe JR, et al. Hypertension and Metabolic Syndrome in Persons with HIV. *Curr Hypertens Rep*. 2020;22(10):78. doi:10.1007/s11906-020-01089-3
20. Todowede OOMS, Sartorius B. Prevalence of metabolic syndrome among HIV-positive and HIV-negative populations in sub-Saharan Africa-a systematic review and meta-analysis. *Systematic Reviews*. 2019;8(1):4. doi:10.1186/s13643-018-0927-y
21. Nix LM, Tien PC. Metabolic syndrome, diabetes, and cardiovascular risk in HIV. *Curr HIV/AIDS Rep*. 2014;11(3):271–278. doi:10.1007/s11904-014-0219-7
22. Mondy K, Overton ET, Grubb J, et al. Metabolic syndrome in HIV-infected patients from an urban, midwestern US outpatient population. *Clin Infect Dis*. 2007;44(5):726–734. doi:10.1086/511679
23. Tu CA, Kuo CF, Lee CM, et al. Prevalence and associated factors of metabolic syndrome among people living with HIV in a medical center of Northern Taiwan. *Sci Rep*. 2025;15(1):4553. doi:10.1038/s41598-025-88552-w
24. Wu PY, Hung CC, Liu WC, et al. Metabolic syndrome among HIV-infected Taiwanese patients in the era of highly active antiretroviral therapy: prevalence and associated factors. *J Antimicrob Chemother*. 2012;67(4):1001–1009. doi:10.1093/jac/dkr558
25. Ang LW, Ng OT, Boudville IC, Leo YS, Wong CS. An observational study of the prevalence of metabolic syndrome in treatment-experienced people living with HIV in Singapore. *PLoS One*. 2021;16(6):e0252320. doi:10.1371/journal.pone.0252320

26. Jantarapakde J, Phanuphak N, Chaturawit C, et al. Prevalence of metabolic syndrome among antiretroviral-naive and antiretroviral-experienced HIV-1 infected Thai adults. *AIDS Patient Care STDS*. 2014;28(7):331–340. doi:10.1089/apc.2013.0294
27. Sashindran VK, Singh AR. A study of effect of anti-retroviral therapy regimen on metabolic syndrome in people living with HIV/AIDS: post hoc analysis from a tertiary care hospital in western India. *Diabetes Metab Syndr*. 2021;15(3):655–659. doi:10.1016/j.dsx.2021.03.003
28. Liu M, He K, Wu Y, et al. Prevalence of, risk factors for, and target organ damage from metabolic syndrome among people living with HIV on ART: a cross-sectional analysis in Chongqing, China. *HIV Med*. 2024;25(5):529–539. doi:10.1111/hiv.13605
29. Abdela AA, Yifter H, Reja A, Ofotokun I, Degu WA. Prevalence and risk factors of metabolic syndrome in Ethiopia: describing an emerging outbreak in HIV clinics of the sub-Saharan Africa - a cross-sectional study. *BMJ Open*. 2023;13(12):e069637. doi:10.1136/bmjopen-2022-069637
30. Husain NE, Noor SK, Elmadhoun WM, et al. Diabetes, metabolic syndrome and dyslipidemia in people living with HIV in Africa: re-emerging challenges not to be forgotten. *HIV AIDS (Auckl)*. 2017;9:193–202. doi:10.2147/HIV.S137974
31. Jaspers Faijer-Westerink H, Kengne AP, Meeks KAC, Agyemang C. Prevalence of metabolic syndrome in sub-Saharan Africa: a systematic review and meta-analysis. *Nutr Metab Cardiovasc Dis*. 2020;30(4):547–565. doi:10.1016/j.numecd.2019.12.012
32. Naidu S, Ponnampalvanar S, Kamaruzzaman SB, Kamarulzaman A. Prevalence of Metabolic Syndrome Among People Living with HIV in Developing Countries: a Systematic Review. *AIDS Patient Care STDS*. 2017;31(1):1–13. doi:10.1089/apc.2016.0140
33. Shakiba M, Shokouhi S, Alaei F, Keyvanfar A, Najafiarab H, Yasaei M. Prevalence of Dysglycemia, Dyslipidemia, and Metabolic Syndrome among Patients with HIV Infection: a Cross-sectional Study from Iran. *Med J Islam Repub Iran*. 2023;37:115. doi:10.47176/mjiri.37.115
34. Dzudzor B, Essel S, Musah L, Agyekum JA, Yeboah K. Metabolic Syndrome and Combination Antiretroviral Therapy in HIV Patients in Periurban Hospital in Ghana: a Case-Control Study. *AIDS Res Treat*. 2023;2023:1566001. doi:10.1155/2023/1566001
35. Mbunkah HA, Meriki HD, Kukwah AT, Nfor O, Nkuo-Akenji T. Prevalence of metabolic syndrome in human immunodeficiency virus - infected patients from the South-West region of Cameroon, using the adult treatment panel III criteria. *Diabetol Metab Syndr*. 2014;6(1):92. doi:10.1186/1758-5996-6-92
36. Hirigo AT, Tesfaye DY. Influences of gender in metabolic syndrome and its components among people living with HIV virus using antiretroviral treatment in Hawassa, southern Ethiopia. *BMC Res Notes*. 2016;9:145. doi:10.1186/s13104-016-1953-2
37. Paula AA, Falcão MC, Pacheco AG. Metabolic syndrome in HIV-infected individuals: underlying mechanisms and epidemiological aspects. *AIDS Res Ther*. 2013;10(1):32. doi:10.1186/1742-6405-10-32
38. Mohan J, Ghazi T, Chuturgoon AA. A Critical Review of the Biochemical Mechanisms and Epigenetic Modifications in HIV- and Antiretroviral-Induced Metabolic Syndrome. *Int J Mol Sci*. 2021;22(21). doi:10.3390/ijms222112020
39. Freiberg MS. HIV and Cardiovascular Disease — an Ounce of Prevention. *The New England Journal of Medicine*. 2023;389(8):760–761. doi:10.1056/NEJMe2306782
40. Virginia AT. HIV infection and coronary heart disease: an intersection of epidemics. *J Infect Dis*. 2012;2012:1.
41. Allison Ross E, Eric GM, Inderjit S, Grace AM. Cardiovascular Disease, Statins, and HIV. *J Infect Dis*. 2016;2016:1.
42. H U, L MT, F B, et al. Assessment of Coronary Artery Disease With Computed Tomography Angiography and Inflammatory and Immune Activation Biomarkers Among Adults With HIV Eligible for Primary Cardiovascular Prevention. *JAMA Network Open*. 2021;4(6):e2114923. doi:10.1001/jamanetworkopen.2021.14923
43. Tseng ZH, Secemsky EA, D D, et al. Sudden cardiac death in patients with human immunodeficiency virus infection. *Journal of the American College of Cardiology*. 2012;59(21):1891–1896. doi:10.1016/j.jacc.2012.02.024
44. Nab N. HIV and myocarditis. Current opinion in HIV and AIDS. 2017;12(6):561–565.
45. De Socio G, Ricci E, Maggi P, et al. Prevalence, awareness, treatment, and control rate of hypertension in HIV-infected patients: the HIV-HY study. *American Journal of Hypertension*. 2014;27(2):222–228. doi:10.1093/ajh/hpt182
46. Jean Joel B, Aude Laetitia N, Jobert RN, et al. Global burden of hypertension among people living with HIV in the era of increased life expectancy: a systematic review and meta-analysis. *J Hypertens*. 2020;38(9):1.
47. Hsue PY, Waters DD. HIV infection and coronary heart disease: mechanisms and management. *Nature Reviews Cardiology*. 2019;16 (12):745–759. doi:10.1038/s41569-019-0219-9
48. A WJ, B JR, K R, T CS, M EO. Human immunodeficiency virus type 1 infection of the brain. *Clin Microbiol Rev*. 1993;6(4):2.
49. Marcus K. HIV's double strike at the brain: neuronal toxicity and compromised neurogenesis. *Front Biosci*. 2007;13(1):2.
50. Sebastian L, Ann Marie N. HIV and the spectrum of human disease. *J Pathol*. 2014;235(2):2.
51. Mirza A, Rathore M. Human immunodeficiency virus and the central nervous system. *Seminars in Pediatric Neurology*. 2012;19(3):119–123. doi:10.1016/j.spen.2012.02.007
52. Cole J, Chin J. HIV infection: a new risk factor for intracerebral hemorrhage? *Neurology*. 2014;83(19):1690–1691. doi:10.1212/WNL.0000000000000967
53. Chow F, He W, Bacchetti P, et al. Elevated rates of intracerebral hemorrhage in individuals from a US clinical care HIV cohort. *Neurology*. 2014;83(19):1705–1711. doi:10.1212/WNL.0000000000000958
54. McIntosh R, Clark U, Cherner M, et al. The Evolution of Assessing Central Nervous System Complications in Human Immunodeficiency Virus: where Do We Go From Here? *The Journal of Infectious Diseases*. 2023;227:S30–S7.
55. Du MWY, Wang Y, Qin C, Mi D, Liu M, Liu J. Prevalence and incidence of stroke among people with HIV. *AIDS*. 2023;37(11):1747–1756. doi:10.1097/QAD.0000000000003632
56. Lake JEOT, Overton T, Naggie S, et al. Expert Panel Review on Nonalcoholic Fatty Liver Disease in Persons With Human Immunodeficiency Virus. *Clinical Gastroenterology and Hepatology: the Official Clinical Practice Journal of the American Gastroenterological Association*. 2022;20(2):256–268. doi:10.1016/j.cgh.2020.10.018
57. Iacob SA, Iacob DG. Non-Alcoholic Fatty Liver Disease in HIV/HBV Patients - a Metabolic Imbalance Aggravated by Antiretroviral Therapy and Perpetuated by the Hepatokine/Adipokine Axis Breakdown. *Front Endocrinol*. 2022;13:814209.
58. Coronel-Castillo CE, Qi X, Contreras-Carmona J, Ramirez-Perez OL, Mendez-Sanchez N. Nonalcoholic fatty liver disease and nonalcoholic steatohepatitis in HIV infection: a metabolic approach of an infectious disease. *Expert Rev Gastroenterol Hepatol*. 2019;13(6):531–540. doi:10.1080/17474124.2019.1599284
59. Manzano-Nunez R, Rivera-Esteban J, Navarro J, et al. Uncovering the NAFLD burden in people living with HIV from high- and middle-income nations: a meta-analysis with a data gap from Subsaharan Africa. *J Int AIDS Soc*. 2023;26(3):e26072. doi:10.1002/jia2.26072

60. P H, C SW, Y C, et al. Predictive factors associated with liver fibrosis and steatosis by transient elastography in patients with HIV mono-infection under long-term combined antiretroviral therapy. *Journal of the International AIDS Society*. 2018;21(11):e25201. doi:10.1002/jia2.25201
61. Enriquez RHM. Ssekubugu R,Nabukalu D,Zeebari Z,Marrone G,Gigante B,Chang LW,Reynolds SJ,Nalugoda F,Ekström AM,Hagström H, Nordenstedt H. Prevalence and risk factors of metabolic dysfunction-associated steatotic liver disease in south Central Uganda: a cross-sectional survey. *Alimentary Pharmacology & Therapeutics*. 2024;59(9):1111–1121.
62. Rockstroh JK. Non-Alcoholic Fatty Liver Disease (NAFLD) and Non-Alcoholic Steatohepatitis (NASH) in HIV. *Current HIV/AIDS Reports*. 2017;14(2):47–53. doi:10.1007/s11904-017-0351-2
63. Kapoor NAJ, Audsley J, Rupali P, Sasadeusz J, Paul TV, Thomas N. A gathering storm: HIV infection and nonalcoholic fatty liver disease in low and middle-income countries. *AIDS*. 2019;33(7):1105–1115. doi:10.1097/QAD.0000000000002161
64. Daultrey HLT, Levett T, Oliver N, Vera AJ, Chakera AJ. HIV and type 2 diabetes: an evolving story. *HIV Medicine*. 2024;25(4):409–423. doi:10.1111/hiv.13595
65. Slama L, Barrett BW, Abraham AG. Risk for incident diabetes is greater in prediabetic men with HIV than without HIV. *AIDS*. 2021;35 (10):1605–1614. doi:10.1097/QAD.0000000000002922
66. Nansseu JR, Bigna JJ, Kaze AD, Noubiap JJ. Incidence and Risk Factors for Prediabetes and Diabetes Mellitus Among HIV-infected Adults on Antiretroviral Therapy: a Systematic Review and Meta-analysis. *Epidemiology*. 2018;29(3):431–441. doi:10.1097/EDE.0000000000000815
67. P A, N H, R S, S S. Prediabetes among HIV-infected individuals receiving antiretroviral therapy: prevalence, diagnostic tests, and associated factors. *AIDS Research and Therapy*. 2020;17(1):25. doi:10.1186/s12981-020-00284-1
68. Todd TB, Stephen RC, Xiuhong L, et al. Antiretroviral therapy and the prevalence and incidence of diabetes mellitus in the multicenter AIDS cohort study. *Arch Intern Med*. 2005;165(10):2.
69. Peer N, Nguyen K, Hill J, et al. Prevalence and influences of diabetes and prediabetes among adults living with HIV in Africa: a systematic review and meta-analysis. *Journal of the International AIDS Society*. 2023;26(3):e26059. doi:10.1002/jia2.26059
70. Prioreschi AMR, Munthali RJ, Soepnel L, et al. Incidence and prevalence of type 2 diabetes mellitus with HIV infection in Africa: a systematic review and meta-analysis. *BMJ open*. 2017;7(3):e013953. doi:10.1136/bmjopen-2016-013953
71. Samuel D-J. HIV therapy and diabetes risk. *Diabetes Care*. 2008;31(6):4.
72. Noubissi EC, Katte J-C, Sobngwi E. Diabetes and HIV. *Current Diabetes Reports*. 2018;18(11):125. doi:10.1007/s11892-018-1076-3
73. Katherine S. Prevalence and pathogenesis of diabetes mellitus in HIV-1 infection treated with combined antiretroviral therapy. *J Acquir Immune Defic Syndr*. 2009;50(5):1.
74. Kathy P, Signe WW, Eric F, et al. Predicting the short-term risk of diabetes in HIV-positive patients: the Data Collection on Adverse Events of Anti-HIV Drugs (D:A:D) study. *J Int AIDS Soc*. 2012;15(2):2.
75. Duale A, David R, Edana C. Examining Relationships between Metabolism and Persistent Inflammation in HIV Patients on Antiretroviral Therapy. *Mediators Inflamm*. 2018;2018(1):1.
76. Stephane DW, Caroline AS, Rainer W, 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.
77. Marcelo NP, Guilherme ZR, Dioze G, et al. Insulin Resistance in HIV-Patients: causes and Consequences. *Front Endocrinol*. 2018;9(1):514.
78. Hasenmajer V, D'Addario NF, Bonaventura I, et al. Breaking Down Bone Disease in People Living with HIV: pathophysiology, Diagnosis, and Treatment. *Adv Exp Med Biol*. 2025;1476:87–110.
79. McGee DM, Cotter AG. HIV and fracture: risk, assessment and intervention. *HIV Med*. 2024;25(5):511–528. doi:10.1111/hiv.13596
80. Anastasia A, Mazzucco W, Pipitò L, et al. Malignancies in people living with HIV: a 25-years observational study from a tertiary hospital in Italy. *J Infect Public Health*. 2025;18(2):102661. doi:10.1016/j.jiph.2025.102661
81. Mathoma A, Sartorius B, Mahomed S, Kane E. The Trends and Risk Factors of AIDS-Defining Cancers and Non-AIDS-Defining Cancers in Adults Living with and without HIV: a Narrative Review. *J Cancer Epidemiol*. 2024;2024:7588928. doi:10.1155/2024/7588928
82. Franzetti M, Ricci E, Bonfanti P. The Pattern of Non-AIDS-defining Cancers in the HIV Population: epidemiology, Risk Factors and Prognosis. A Review. *Curr HIV Res*. 2019;17(1):1–12. doi:10.2174/1570162X17666190327153038
83. Rickabaugh TM, Baxter RM, Sehl M, et al. Acceleration of age-associated methylation patterns in HIV-1-infected adults. *PLoS One*. 2015;10 (3):e0119201. doi:10.1371/journal.pone.0119201
84. Gross AM, Jaeger PA, Kreisberg JF, et al. Methylome-wide Analysis of Chronic HIV Infection Reveals Five-Year Increase in Biological Age and Epigenetic Targeting of HLA. *Mol Cell*. 2016;62(2):157–168. doi:10.1016/j.molcel.2016.03.019
85. Watanabe M, Jergovic M, Davidson L, et al. Inflammatory and immune markers in HIV -infected older adults on long-term antiretroviral therapy: persistent elevation of sCD14 and of proinflammatory effector memory T cells. *Aging Cell*. 2022;21(9):e13681. doi:10.1111/acel.13681
86. Deeks SG. HIV infection, inflammation, immunosenescence, and aging. *Annu Rev Med*. 2011;62(1):141–155. doi:10.1146/annurev-med -042909-093756
87. Desai S, Landay A. Early immune senescence in HIV disease. *Curr HIV/AIDS Rep*. 2010;7(1):4–10. doi:10.1007/s11904-009-0038-4
88. Hearps AC, Angelovich TA, Jaworowski A, Mills J, Landay AL, Crowe SM. HIV infection and aging of the innate immune system. *Sexual Health*. 2011;8(4):453–464. doi:10.1071/SH11028
89. Fülöp T, Herbein G, Cossarizza A, et al. Cellular Senescence, Immunosenescence and HIV. *Interdiscip Top Gerontol Geriatr*. 2017;42:28–46.
90. French M, King M, Tschampa J, da Silva BA, Landay A. Serum Immune Activation Markers Are Persistently Increased in Patients with HIV Infection after 6 Years of Antiretroviral Therapy despite Suppression of Viral Replication and Reconstitution of CD4 + T Cells. *The Journal of Infectious Diseases*. 2009;200(8):1212–1215. doi:10.1086/605890
91. Kuller LH, T R, B W, et al. Inflammatory and coagulation biomarkers and mortality in patients with HIV infection. *PLoS medicine*. 2008;5(10): e203. doi:10.1371/journal.pmed.0050203
92. Damouche A, Lazure T, Avettand-Fènoël V, et al. Adipose Tissue Is a Neglected Viral Reservoir and an Inflammatory Site during Chronic HIV and SIV Infection. *PLoS Pathogens*. 2015;11(9):e1005153. doi:10.1371/journal.ppat.1005153
93. Micaela I, Michael S, Sahar S et al. Coronary artery endothelial dysfunction is present in HIV-positive individuals without significant coronary artery disease. *AIDS*. 2017;31(9):1281.
94. Rickabaugh TM, Kilpatrick RD, Hultin LE, et al. The Dual Impact of HIV-1 Infection and Aging on Naïve CD4+ T-Cells: additive and Distinct Patterns of Impairment. *PLoS One*. 2011;6(1):e16459. doi:10.1371/journal.pone.0016459

95. Sokoya T, Steel HC, Nieuwoudt M, Rossouw TM. HIV as a Cause of Immune Activation and Immunosenescence. *Mediators Inflamm*. 2017;2017:6825493. doi:10.1155/2017/6825493
96. Gabuzda D, Jamieson BD, Collman RG, et al. Pathogenesis of Aging and Age-related Comorbidities in People with HIV: highlights from the HIV ACTION Workshop. *Pathog Immun*. 2020;5(1):143–174. doi:10.20411/pai.v5i1.365
97. He N. Research Progress in the Epidemiology of HIV/AIDS in China. *<![CDATA[China CDC Weekly]]>*. 2021;3(48):1022–1030. doi:10.46234/ccdcw2021.249
98. Cotto B, Natarajanseenivasan K, Langford D. HIV-1 infection alters energy metabolism in the brain: contributions to HIV-associated neurocognitive disorders. *Prog Neurobiol*. 2019;181:101616. doi:10.1016/j.pneurobio.2019.101616
99. Guzmán-Fulgencio M, Berenguer J, Micheloud D, et al. European mitochondrial haplogroups are associated with CD4+ T cell recovery in HIV-infected patients on combination antiretroviral therapy. *J Antimicrob Chemother*. 2013;68(10):2349–2357. doi:10.1093/jac/dkt206
100. Willig AL, Overton ET. Metabolic Complications and Glucose Metabolism in HIV Infection: a Review of the Evidence. *Curr HIV/AIDS Rep*. 2016;13(5):289–296. doi:10.1007/s11904-016-0330-z
101. Gangcuangco LMA, Mitchell BI, Siriwardhana C, et al. Mitochondrial oxidative phosphorylation in peripheral blood mononuclear cells is decreased in chronic HIV and correlates with immune dysregulation. *PLoS One*. 2020;15(4):e0231761. doi:10.1371/journal.pone.0231761
102. Kanmogne GD. HIV Infection, Antiretroviral Drugs, and the Vascular Endothelium. *Cells*. 2024;13(8):672. doi:10.3390/cells13080672
103. Arnaiz de Las RevillasF, Gonzalez-Quintanilla V, Parra JA, PalaciosE, Gonzalez-Rico C, Armiñanzas C, Gutiérrez-Cuadra M, Oterino A, Fariñas-Alvarez C, Fariñas, MC. Evaluation of endothelial function and subclinical atherosclerosis in patients with HIV infection. *Sci Rep*. 2021;11(1). doi:10.1038/s41598-021-97795-2
104. Andrew Weil S, Charles B, Alice B, et al. Serum E-selectin and endothelial cell-specific Molecule-1 levels among people living with HIV on long term ART in Uganda: a pilot cross-sectional study. *AIDS Res Ther*. 2023;20(1):26.
105. Roseline A, Delphine G, Gérard Menan K, et al. Plasma sVCAM-1, antiretroviral therapy and mortality in HIV-1-infected West African adults. *HIV Med*. 2022;23(7):717–726.
106. Genevieve M, Nereshni L, Catherine W, et al. Biomarkers of Endothelial Activation in Black South African HIV-Positive Subjects are Associated with Both High Viral Load and Low CD4 Counts. *AIDS Res Hum Retroviruses*. 2022;38(2):152–161.
107. OH JA, D E, Mmp G, et al. The effect of initiation of antiretroviral therapy on monocyte, endothelial and platelet function in HIV-1 infection. *HIV Med*. 2015;16(10):608–619.
108. Baker JVDD, Rapkin J, Hullsiek KH, et al. Untreated HIV infection and large and small artery elasticity. *Journal of Acquired Immune Deficiency Syndromes*. 2009;52(1):25–31. doi:10.1097/QAI.0b013e3181b02e6a
109. Paweł B, Tomasz M, Michał P, et al. Evaluation of endothelial function and arterial stiffness in HIV-infected patients: a pilot study. *Kardiol Pol*. 2014;73(5):344.
110. Christine K, Henry CM, Robert SH, et al. HIV-Related Arterial Stiffness in Malawian Adults Is Associated With the Proportion of PD-1-Expressing CD8+ T Cells and Reverses With Antiretroviral Therapy. *J Infect Dis*. 2019;219(12):1948–1958.
111. Longa K, Fastone G, Chris G, et al. Immune activation and arterial stiffness in lean adults with HIV on antiretroviral therapy. *South Afr J HIV Med*. 2021;22(1):1.
112. John RK. Adipose Tissue in HIV Infection. *Compr Physiol*. 2017;7(4):1339–57.
113. DK K, V M, ED M, et al. Dyslipidemia in Human Immunodeficiency Virus Disease: JACC Review Topic of the Week. *Journal of the American College of Cardiology*. 2023;82(2):171–181. doi:10.1016/j.jacc.2023.04.050
114. Lianfeng L, Yang Y, Zhangong Y, et al. Altered plasma metabolites and inflammatory networks in HIV-1 infected patients with different immunological responses after long-term antiretroviral therapy. *Front Immunol*. 2023;14(1):1254155.
115. Peltenburg NC, Schoeman JC, Hou J, et al. Persistent metabolic changes in HIV-infected patients during the first year of combination antiretroviral therapy. *Sci Rep*. 2018;8(1):16947. doi:10.1038/s41598-018-35271-0
116. Neeti A, Dinakar I, Sanjeet GP, et al. HIV-1 Vpr induces adipose dysfunction in vivo through reciprocal effects on PPAR/GR co-regulation. *Sci Transl Med*. 2013;5(213):213ra164.
117. Gorwood JBC, Mantecon M, Atlan M, et al. Impact of HIV/simian immunodeficiency virus infection and viral proteins on adipose tissue fibrosis and adipogenesis. *AIDS*. 2019;33(6):953–964. doi:10.1097/QAD.0000000000002168
118. G C, P M, D W, S JK, J P, F KR. Lipids, lipoproteins, triglyceride clearance, and cytokines in human immunodeficiency virus infection and the acquired immunodeficiency syndrome. *The Journal of Clinical Endocrinology and Metabolism*. 1992;74(5):1045–1052. doi:10.1210/jcem.74.5.1373735
119. Kelesidis T, Currier JS. Dyslipidemia and cardiovascular risk in human immunodeficiency virus infection. *Endocrinol Metab Clin North Am*. 2014;43(3):665–684. doi:10.1016/j.ecl.2014.06.003
120. Roesch F, Richard L, Rua R, Porrot F, Casartelli N, Schwartz O. Vpr Enhances Tumor Necrosis Factor Production by HIV-1-Infected T Cells. *J Virol*. 2015;89(23):12118–12130. doi:10.1128/JVI.02098-15
121. Zhao X, An X, Yang C, Sun W, Ji H, Lian F. The crucial role and mechanism of insulin resistance in metabolic disease. *Front Endocrinol (Lausanne)*. 2023;14:1149239. doi:10.3389/fendo.2023.1149239
122. Reaven GM. Banting lecture 1988. Role of insulin resistance in human disease. *Diabetes*. 1988;37(12):1595–1607. doi:10.2337/diab.37.12.1595
123. Reaven GM. The role of insulin resistance and hyperinsulinemia in coronary heart disease. *Metabolism*. 1992;41(5 Suppl 1):16–19. doi:10.1016/0026-0495(92)90088-R
124. M M, S M, B P. You Are What You Eat-The Relationship between Diet, Microbiota, and Metabolic Disorders-A Review. *Nutrients*. 2020;12(4):1.
125. Q R, N E, E B, et al. Exercise training modulates the gut microbiota profile and impairs inflammatory signaling pathways in obese children. *Experimental & Molecular Medicine*. 2020;52(7):1048–1061. doi:10.1038/s12276-020-0459-0
126. Aisha N, Olivia C, Wendy ND-B, et al. Exposure to HIV-1 directly impairs mucosal epithelial barrier integrity allowing microbial translocation. *PLoS Pathog*. 2010;6(4):e1000852.
127. FC N, A E, W R, R K. Gut Microbiota in HIV Infection: implication for Disease Progression and Management. *Gastroenterology Research and Practice*. 2014;2014:803185. doi:10.1155/2014/803185
128. Troels Bygum K, Gideon E, Janne P, et al. Plasma Soluble CD163 Level Independently Predicts All-Cause Mortality in HIV-1-Infected Individuals. *J Infect Dis*. 2016;214(8):1198–1204.
129. Giulia M, Camilla T, Guido S. Microbial translocation in the pathogenesis of HIV infection and AIDS. *Clin Microbiol Rev*. 2013;26(1):2–18.

130. Beom Seok P, Jie-Oh L. Recognition of lipopolysaccharide pattern by TLR4 complexes. *Exp Mol Med*. 2013;45(12):e66.
131. Brenchley JM, Schacker TW, Ruff LE, et al. CD4+ T cell depletion during all stages of HIV disease occurs predominantly in the gastrointestinal tract. *J Exp Med*. 2004;200(6):749–759. doi:10.1084/jem.20040874
132. Vujkovic-Cvijin I, Dunham RM, Iwai S, et al. Dysbiosis of the gut microbiota is associated with HIV disease progression and tryptophan catabolism. *Sci Transl Med*. 2013;5(193):193ra91. doi:10.1126/scitranslmed.3006438
133. Sereti I, Verburgh ML, Gifford J, et al. Impaired gut microbiota-mediated short-chain fatty acid production precedes morbidity and mortality in people with HIV. *Cell Rep*. 2023;42(11):113336. doi:10.1016/j.celrep.2023.113336
134. Vázquez-Castellanos JF, Serrano-Villar S, Jiménez-Hernández N, et al. Interplay between gut microbiota metabolism and inflammation in HIV infection. *Isme J*. 2018;12(8):1964–1976. doi:10.1038/s41396-018-0151-8
135. Villanueva-Millán MJ, Pérez-Matute P, Recio-Fernández E, Lezana Rosales JM, Oteo JA. Characterization of gut microbiota composition in HIV-infected patients with metabolic syndrome. *J Physiol Biochem*. 2019;75(3):299–309. doi:10.1007/s13105-019-00673-9
136. Kauder SE, Bosque A, Lindqvist A, Planelles V, Verdin E, Ross S. Epigenetic regulation of HIV-1 latency by cytosine methylation. *PLoS Pathog*. 2009;5(6):e1000495. doi:10.1371/journal.ppat.1000495
137. Jochems SP, Jacquelin B, Tchitchek N, et al. DNA methylation changes in metabolic and immune-regulatory pathways in blood and lymph node CD4 + T cells in response to SIV infections. *Clin Epigenetics*. 2020;12(1):188. doi:10.1186/s13148-020-00971-w
138. Vanhamel J, Bruggemans A, Debyser Z. Establishment of latent HIV-1 reservoirs: what do we really know? *J Virus Erad*. 2019;5(1):3–9. doi:10.1016/S2055-6640(20)30275-2
139. P R, S J, G M, R J, M M. Incidence and prevalence of the metabolic syndrome in a cohort of naive HIV-infected patients: prospective analysis at 48 weeks of highly active antiretroviral therapy. *Int J STD AIDS*. 2007;18(3):184–187.
140. Z S, S L, C N, et al. Immune Activation, Inflammation, and Non-AIDS Co-Morbidities in HIV-Infected Patients under Long-Term ART. *Viruses*. 2019;11(3):1.
141. Margolis AM, Heverling H, Pham PA, Stolbach A. A review of the toxicity of HIV medications. *J Med Toxicol*. 2014;10(1):26–39. doi:10.1007/s13181-013-0325-8
142. Ryom L, Cotter A, De Miguel R. 2019 update of the European AIDS Clinical Society Guidelines for treatment of people living with HIV version 10.0. *HIV Medicine*. 2020;21(10):617–624. doi:10.1111/hiv.12878
143. Symington B, Mapanga RF, Norton GR, Essop MF. Resveratrol Co-Treatment Attenuates the Effects of HIV Protease Inhibitors on Rat Body Weight and Enhances Cardiac Mitochondrial Respiration. *PLoS One*. 2017;12(1):e0170344. doi:10.1371/journal.pone.0170344
144. H C, M JB, C C, et al. Metabolic abnormalities and cardiovascular disease risk factors in adults with human immunodeficiency virus infection and lipodystrophy. *Clinical Infectious Diseases: an Official Publication of the Infectious Diseases Society of America*. 2001;32(1):130–139. doi:10.1086/317541
145. ER F, PW M. HIV and HAART-Associated Dyslipidemia. *The Open Cardiovascular Medicine Journal*. 2011;5:49–63. doi:10.2174/1874192401105010049
146. B G, I G. Metabolic syndrome associated with HIV and highly active antiretroviral therapy. *Current diabetes Reports*. 2009;9(1):37–42. doi:10.1007/s11892-009-0008-7
147. Risheng C, Yiqiao H, Yun W, et al. Prevention of HIV protease inhibitor-induced dysregulation of hepatic lipid metabolism by raltegravir via endoplasmic reticulum stress signaling pathways. *J Pharmacol Exp Ther*. 2010;334(2):3.
148. Thet D, Siritientong T. Antiretroviral Therapy-Associated Metabolic Complications: review of the Recent Studies. *HIV AIDS (Auckl)*. 2020;12:507–524. doi:10.2147/HIV.S275314
149. Tanaka T, Nakazawa H, Kuriyama N, Kaneki M. Farnesyltransferase inhibitors prevent HIV protease inhibitor (lopinavir/ritonavir)-induced lipodystrophy and metabolic syndrome in mice. *Exp Ther Med*. 2018;15(2):1314–1320. doi:10.3892/etm.2017.5526
150. L C, B V, G J, et al. Metabolic complications affecting adipose tissue, lipid and glucose metabolism associated with HIV antiretroviral treatment. *Expert Opinion on Drug Safety*. 2019;18(9):829–840. doi:10.1080/14740338.2019.1644317
151. Wang X, Howell D, Tang L, Shao J, Ye Z. Comparative study on prevalence of metabolic syndrome based on three criteria among adults in Zhejiang province, China: an observational study. *BMJ Open*. 2020;10(4):e035216. doi:10.1136/bmjopen-2019-035216
152. H T, R BS, K JR, et al. Relationships Between Adipose Mitochondrial Function, Serum Adiponectin, and Insulin Resistance in Persons With HIV After 96 Weeks of Antiretroviral Therapy. *Journal of Acquired Immune Deficiency Syndromes*. 2019;80(3):358–366. doi:10.1097/QAI.0000000000001926
153. Triant VA, Perez J, Regan S. Cardiovascular Risk Prediction Functions Underestimate Risk in HIV Infection. *Circulation*. 2018;137(21):2203–2214. doi:10.1161/CIRCULATIONAHA.117.028975
154. Achhra AC, Lyass A, Borowsky L, et al. Assessing Cardiovascular Risk in People Living with HIV: current Tools and Limitations. *Curr HIV/AIDS Rep*. 2021;18(4):271–279. doi:10.1007/s11904-021-00567-w
155. Milinkovic APB, Mazziteli M, Girometti N, Asboe D, Pozniak A, Boffito M. Delivering specialised care to people ageing with HIV in the UK: experience and evolution of services from 2009 to 2019. *The Lancet HIV*. 2022;9(Suppl 1):S1. doi:10.1016/S2352-3018(22)00066-2
156. Rennatus M, Emma LF, Shanta RD, et al. Cigarette smoking prevalence among adults with HIV compared with the general adult population in the United States: cross-sectional surveys. *Ann Intern Med*. 2015;162(5):1.
157. Shokoohi M, Bauer G, Kaida A, et al. Substance use patterns among women living with HIV compared with the general female population of Canada. *Drug and Alcohol Dependence*. 2018;191:70–77. doi:10.1016/j.drugalcdep.2018.06.026
158. Frazier E, Sutton M, Brooks J, Shouse R, Weiser J. Trends in cigarette smoking among adults with HIV compared with the general adult population, United States - 2009-2014. *Preventive Medicine*. 2018;111:231–234. doi:10.1016/j.ypmed.2018.03.007
159. A D, R B, T S, et al. Prevalence and predictors of cigarette smoking among people with HIV in Western Jamaica. *AIDS Care*. 2024;2014:1–9.
160. KP R, RA P, L E, et al. Impact of Cigarette Smoking and Smoking Cessation on Life Expectancy Among People With HIV: a US-Based Modeling Study. *The Journal of Infectious Diseases*. 2016;214(11):1672–1681. doi:10.1093/infdis/jiw430
161. M M, C CD, K S, M D, S F. HIV and alcohol misuse among miners in Zimbabwe. *Lancet*. 2025;404(10471):2538.
162. P K, Smoking MGL. alcohol and illicit drug use effects on survival in HIV-positive persons. *Current Opinion in HIV and AIDS*. 2016;11(5):514–520. doi:10.1097/COH.0000000000000306

163. PS S, K A. HIV-1 and alcohol: interactions in the central nervous system. *Alcoholism, Clinical and Experimental Research*. 2014;38 (3):604–610. doi:10.1111/acer.12282
164. EJ E, EC W, M BDL. Addressing unhealthy alcohol use among people living with HIV: recent advances and research directions. *Current Opinion in Infectious Diseases*. 2018;31(1):1–7. doi:10.1097/QCO.0000000000000422
165. Vincenzo G, Luigi G, Rebecca R, et al. Healthy Promotion for Fighting Metabolic Syndrome: insights from Multi-Center HeRO-FiT Cohort. *Int J Environ Res Public Health*. 2020;17(15):2.
166. Singhato A, Booranasuksakul U, Khongkhon S, Rueangsri N. Effectiveness of the Therapeutic Lifestyle Change Diet Intervention to Improve Biochemical Markers of Cardiovascular Diseases in HIV-Infected Patients with Dyslipidemia. *Annals of Nutrition & Metabolism*. 2024;80 (4):202–210. doi:10.1159/000538578
167. Esther UA, Emmanuel Ifeanyi O, Okechukwu PCU, Awotunde OS, Adeyinka OA, Mariam OA. Inclusion of nutritional counseling and mental health services in HIV/AIDS management: a paradigm shift. *Medicine (Baltimore)*. 2023;102(41):1.
168. B D, L OS, T Y, S G. Potential Advantages of a Well-balanced Nutrition Regimen for People Living with Human Immunodeficiency Virus Type −1. *Journal of AIDS and HIV Treatment*. 2024;6(1):11–27. doi:10.33696/AIDS.6.048
169. Rosmeri KL, Regina K, Eduardo S, Carísi AP, Jorge PR. Dietary intervention prevents dyslipidemia associated with highly active antiretroviral therapy in human immunodeficiency virus type 1-infected individuals: a randomized trial. *J Am Coll Cardiol*. 59(11):1.
170. IO O, D A, B S, H J. Diet quality, food insecurity and risk of cardiovascular diseases among adults living with HIV/AIDS: a scoping review protocol. *BMJ open*. 2021;11(10):e047314. doi:10.1136/bmjopen-2020-047314
171. Martemucci G, Fracchiolla G, Muraglia M, Tardugno R, Dibenedetto RS, D'Alessandro AG. Metabolic Syndrome: a Narrative Review from the Oxidative Stress to the Management of Related Diseases. *Antioxidants (Basel)*. 2023;12(12). doi:10.3390/antiox12122091
172. S C-B, AM R-L, M S-P, E R, C R. Dietary Strategies for Metabolic Syndrome: a Comprehensive Review. *Nutrients*. 2020;12(10):1.
173. GA H, GW L, JR J, WD D. Impact of Aerobic and Resistance Exercise on the Health of HIV-Infected Persons. *American Journal of Lifestyle Medicine*. 2009;3(6):489–499. doi:10.1177/1559827609342198
174. Jones R, Robinson AT, Beach LB, et al. Exercise to Prevent Accelerated Vascular Aging in People Living With HIV. *Circ Res*. 2024;134 (11):1607–1635. doi:10.1161/CIRCRESAHA.124.323975
175. Matthew JF, Priscilla YH, Laura AB, et al. Characteristics, Prevention, and Management of Cardiovascular Disease in People Living With HIV: a Scientific Statement From the American Heart Association. *Circulation*. 2019;140(2):1.
176. Grinspoon SK, Fitch KV, Zanni MV, et al. Pitavastatin to Prevent Cardiovascular Disease in HIV Infection. *The New England Journal of Medicine*. 2023;389(8):687–699. doi:10.1056/NEJMoa2304146
177. KM E, J Y, SM D, GA M. Rosuvastatin Worsens Insulin Resistance in HIV-Infected Adults on Antiretroviral Therapy. *Clinical Infectious Diseases: an Official Publication of the Infectious Diseases Society of America*. 2015;61(10):1566–1572. doi:10.1093/cid/civ554
178. Waters D, Ho J, Boekholdt S, et al. Cardiovascular event reduction versus new-onset diabetes during atorvastatin therapy: effect of baseline risk factors for diabetes. *Journal of the American College of Cardiology*. 2013;61(2):148–152. doi:10.1016/j.jacc.2012.09.042
179. Sattar N, Preiss D, Murray H, et al. Statins and risk of incident diabetes: a collaborative meta-analysis of randomised statin trials. *Lancet*. 2010;375(9716):735–742. doi:10.1016/S0140-6736(09)61965-6
180. L J. Dyslipidemia and lipid management in HIV-infected patients. *Current Opinion in Endocrinology, Diabetes, and Obesity*. 2011;18 (2):144–147. doi:10.1097/MED.0b013e328344556e
181. V P. Statin use in people living with HIV. *The Lancet Infectious Diseases*. 2023;23(7):789. doi:10.1016/S1473-3099(23)00382-1
182. Panel on antiretroviral guidelines for adults and adolescents. Guidelines for the use of antiretroviral agents in adults and adolescents with HIV [Internet]. Department of Health and Human Services. https://clinicalinfo.hiv.gov/en/guidelines/hiv-clinical-guidelines-adult-and-adolescent-arv/statin-therapy-people-hiv?view=full. 2024 Sep 12 [cited Sep 12]. Available from 2024.
183. Franck B, Princy NK, Bruno C, et al. Evolocumab in HIV-Infected Patients With Dyslipidemia: primary Results of the Randomized, Double-Blind BEIJERINCK Study. *J Am Coll Cardiol*. 75(20):1.
184. Gutierrez AD, Balasubramanyam A. Dysregulation of glucose metabolism in HIV patients: epidemiology, mechanisms, and management. *Endocrine*. 2012;41(1):1–10. doi:10.1007/s12020-011-9565-z
185. Nimitphong H, Jiriyasin S, Kasemasawachanon P, Sungkanuparph S. Metformin for Preventing Progression From Prediabetes to Diabetes Mellitus in People Living With Human Immunodeficiency Virus. *Cureus*. 2022;14(4):e24540. doi:10.7759/cureus.24540
186. Albuquerque R, Faria JLR, Pavão DM. Letter to the Editor Regarding the Article: radiographic Evaluation of Postoperative Alignment in Total Knee Arthroplasty. *Rev Bras Ortop*. 2021;56(6):819–820.
187. Armah KA, Chang CC, Baker JV, et al. Prehypertension, hypertension, and the risk of acute myocardial infarction in HIV-infected and -uninfected veterans. *Clin Infect Dis*. 2014;58(1):121–129. doi:10.1093/cid/cit652
188. Gandhi R, Bedimo R, Hoy J, et al. Antiretroviral Drugs for Treatment and Prevention of HIV Infection in Adults: 2022 Recommendations of the International Antiviral Society-USA Panel. *JAMA*. 2023;329(1):63–84. doi:10.1001/jama.2022.22246
189. JY CS, Lin X, Chen H, et al. Estimated Pulse Wave Velocity as a Novel Non-Invasive Biomarker for Metabolic Syndrome Among People Living with HIV. *Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy*. 2024;17:1999–2010. doi:10.2147/DMSO.S452498
190. Lui LH, Lee J, CK W, et al. An efficient approach to estimate the risk of coronary artery disease for people living with HIV using machine-learning-based retinal image analysis. *PLoS One*. 2023;18(2):e0281701. doi:10.1371/journal.pone.0281701
191. El-Far M, Tremblay CL. Gut microbial diversity in HIV infection post combined antiretroviral therapy: a key target for prevention of cardiovascular disease. *Curr Opin HIV AIDS*. 2018;13(1):38–44. doi:10.1097/COH.0000000000000426
192. Yang Q, Zaongo SD, Zhu L, Yan J, Yang J, Ouyang J. The Potential of Clostridium butyricum to Preserve Gut Health, and to Mitigate Non-AIDS Comorbidities in People Living with HIV. *Probiotics Antimicrob Proteins*. 2024;16(4):1465–1482. doi:10.1007/s12602-024-10227-1
193. Geng ST, Zhang ZY, Wang YX, et al. Regulation of Gut Microbiota on Immune Reconstitution in Patients With Acquired Immunodeficiency Syndrome. *Front Microbiol*. 2020;11:594820. doi:10.3389/fmicb.2020.594820
194. Xian QF, Liu Y, Zou W, Wang J. Research progress of Chinese medicine treatment of HAART-related hyperlipidemia. *Zhongguo Zhong Yao Za Zhi*. 2013;38(15):2530–2533.
195. Shahrajabian MH, Sun W. The Importance of Traditional Chinese Medicine in the Intervention and Treatment of HIV while Considering its Safety and Efficacy. *Curr HIV Res*. 2023;21(6):331–346. doi:10.2174/011570162X271199231128092621

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