



Menopause experiences among women living with HIV (WLHIV) in Sub-Saharan Africa: a scoping review

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Abstract:

Background:

Menopause is a significant biological transition for women living with HIV (WLHIV) in Sub-Saharan Africa (SSA), presenting unique challenges such as increased risks for bone loss and more severe symptoms. With increasing life expectancy due to effective antiretroviral therapy (ART), the population of ageing WLHIV continues to grow, requiring tailored HIV services. However, research on the complex association between HIV and menopause remains limited.

Objectives:

This scoping review aims to provide a comprehensive overview of current knowledge on menopause among WLHIV in Sub-Saharan Africa, identify gaps in existing literature, and provide insights for future research and interventions.

Methods:

A scoping review was conducted following the JBI framework and PRISMA-ScR guidelines. Databases PubMed, Science Direct and Google Scholar were searched for studies published in English up to October 2023. Eligible studies included perimenopausal and postmenopausal WLHIV in Sub-Saharan Africa. Data were extracted and summarised based on study characteristics, methodology, menopause definitions, symptoms, and health outcomes.

Results:

A total of 138 articles were identified and screened for eligibility based on titles and abstracts; 72 articles were assessed for full-text eligibility, and 65 articles were excluded. Seven studies in South Africa, Nigeria, and Zimbabwe met the final inclusion criteria. Studies found a higher prevalence of early menopause, decreased bone mineral density, and more severe menopausal symptoms among WLHIV compared to women living without HIV. Furthermore, several studies reported a high BMI was strongly associated with symptom severity.

Conclusion:

Our scoping review highlights a significant association between HIV and menopause among WLHIV in Sub-Saharan Africa. WLHIV experience severe menopausal symptoms, earlier menopause, and lower bone mineral density compared to women without HIV. However, research is limited, and findings are inconsistent. Future longitudinal studies are required to understand the complex relationship between menopause and HIV for the development of effective interventions. Integrating menopause care into HIV services is crucial for improving health outcomes and quality of life among WLHIV in this region.

Keywords: Menopause, HIV, Women living with HIV, WLHIV, Sub-Saharan Africa

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1. Introduction

1.1 Background:

The World Health Organization (WHO) reported that by 2023, 39.9 million individuals living with HIV globally, including 20.5 million women aged 15 and older (1,2). Sub-Saharan Africa continues to have the highest HIV burden in the world, with over 20.8 million people living with HIV (2,3), of which 3 million are aged 50 and above (4). In 2023, women and girls accounted for 44% of all new HIV infections, contributing a considerable proportion of the HIV population (2).

The introduction of antiretroviral therapy (ART) in Sub-Saharan Africa has significantly improved survival rates (5), transforming HIV from a potentially life-threatening disease into a manageable chronic condition (6), leading to normal life expectancy comparable to women living in highly developed countries (7,8). However, as life expectancy increases, more WLHIV are reaching middle-age (9), experiencing age-related conditions and biological transitions such as menopause, due to the effectiveness of ART in prolonging their lives (4,6).

Menopause is a natural biological transition defined as the permanent cessation of menstruation after 12 consecutive months of amenorrhea (10,11). The onset of menopause is marked by a decline in estrogen levels, leading to various physical and psychological symptoms (6,11). Menopause affects mood and sexual function, negatively impacts bone health and cognitive function, and increases the risk of osteoporosis, cardiovascular disease, and decreased bone mineral density in both WLHIV and women living without HIV (WLWOH) (12–14). However, WLHIV have a higher prevalence of age-related comorbidities, including metabolic disorders, compared to WLWOH (6). Menopause can accelerate the onset, development, and progression of these comorbidities (6,15), which may be worsened by HIV or its treatment (6). The complex bidirectional relationship between HIV and menopause affects the natural history, progression, symptoms, and complications associated with menopause, while menopause may also influence the trajectory of HIV infections (12,16). Both HIV and menopause manifest overlapping symptoms, including fatigue, cognitive changes, and mood disturbances, making it difficult to distinguish whether symptoms are attributable to HIV infection or the menopausal transition (16). Common menopausal symptoms including mood swings, irregular sleep patterns, cognitive dysfunction, vasomotor symptoms (including hot flashes and night sweats), urogenital issues (such as vaginal dryness and sexual dysfunction), urinary complications, physical discomforts (including joint and muscle pain), body temperature fluctuations, and fatigue are reported by both HIV-positive and HIV-negative women worldwide (11,17–21). In a UK PRIME, joint pain was reported as the most common symptom (66.4%), hot flashes (63.0%), fatigue (61.6%), sleep irregularities (61.4%), and vaginal dryness (34.0%) (11). Among rural Xhosa postmenopausal women, hot flashes were the most prevalent symptom, reported by 80% of participants (22). In Nigeria, the most frequently reported symptoms included body and joint pains (58.4%), hot flashes (49.8%), and urine symptoms (28.7%) (23). Ghanaian women reported

experiencing fatigue (79.9%), insomnia (71.0%), heart palpitations (63.7%), weight gain (61.8%), hot flushes (56.5%), and irritability (56.5%) during menopause (24). An Ethiopian study further indicated that hot flushes (65.9%), insomnia (49.6%), depressive mood (46.0%), irritability (45.1%), anxiety (39.8%), and urogenital problems (30.5%) were prevalent among WLHIV (25).

Symptom severity can vary between HIV-positive women and HIV-negative women (17), with studies indicating that WLHIV may experience an earlier onset of menopause, along with more severe symptoms (5,17,21,26,27) compared to HIV-negative women, particularly in the somatic and psychological domains (28). Furthermore, menopausal symptoms can significantly affect the quality of life for WLHIV (15), potentially impacting HIV progression and adherence to ART (16,17,29,30). Several studies have investigated whether ART modifies the effect of HIV infection on menopausal timing or symptom severity, although findings remain inconsistent. A systematic review highlighted methodological limitations and found no definite evidence that HIV or ART accelerates menopause onset (31). However, symptom burden may still interact with HIV care, as some studies suggest that severe menopausal symptoms are associated with poorer ART adherence and clinic attendance (32). The overlap of symptoms between HIV and menopause complicates healthcare providers' ability to identify underlying causes and deliver appropriate treatment (11), leading to new complexities in patient care and disease management (17). While ART has advanced survival rates for WLHIV, its influence on menopause symptom severity and timing remains uncertain, indicating the need for comprehensive longitudinal studies using validated measures.

In addition to HIV-related factors, lifestyle factors such as smoking and obesity can influence menopausal timing in the general population (33). However, the evidence on their interaction in WLHIV remains inconclusive. Some studies indicate no significant association between lifestyle factors and early menopause, after adjusting for HIV-related markers such as viral suppression, viral load, CD4 cell count, and ART use (19,34,35), while other studies identify low CD4 cell counts as a potential risk factor (36–38). Some suggest that higher CD4 cell counts may be associated with increased vasomotor symptoms (39,40). Although these findings are inconclusive, this highlights an important research gap in SSA, where the combined effects of lifestyle and HIV-related risk factors on menopausal timing and symptom severity have not been studied.

Menopause is a unique experience for each woman (17), with diverse experiences reported across various ethnic groups and populations (41). However, there exists limited research associating menopausal symptoms with ethnicity or country of origin, especially in low and middle-income countries (25). The age at which natural menopause occurs varies among different populations, with the earliest onset observed in African, Latin American, Asian, and Middle Eastern countries, and the highest found in Europe, Australia, and the United States (33). In developed countries, the average age for natural menopause is typically around 50 to 52 years (12). In contrast, WLHIV tend to

experience menopause at a younger median age of 47.5 to 50 years (15,19,20,34,36,42). WLHIV may encounter ovarian dysfunction earlier than their HIV-negative counterparts, contributing to an earlier onset of menopause (43).

Research on the effects of menopause on HIV disease progression and the influence of HIV infection on menopause is limited (34), especially in Sub-Saharan Africa (44). Most studies focusing on menopause among WLHIV are from North America and Europe, predominantly involving Caucasian women from high-income countries. There is a significant lack of empirical research on women in low- and middle-income countries, particularly in Sub-Saharan Africa (28,45–48). Women are often underrepresented and excluded from specific areas of HIV clinical research (6,49,50). Studies often focus on pregnancy-related reproductive health issues, resulting in significant gaps in the literature, particularly for WLHIV over the age of 50 (6,35,50). The lack of standardised data on menopausal symptoms within HIV cohorts makes it difficult to obtain convincing evidence (51). Furthermore, many studies lack sufficient statistical power, leading to limitations and gaps in understanding (50), despite significant advancements in the diagnosis and treatment of HIV (50).

The existing literature on menopause in women living with HIV in Sub-Saharan Africa is limited, despite the region carrying the largest burden of HIV globally and a growing population of women ageing with HIV. The increasing life expectancy of HIV-positive women highlights the challenges of ageing and menopause (52,53), which may intensify health inequalities and impact overall quality of life. Further research is required to understand the unique challenges faced by WLHIV and address disparities in access to menopausal healthcare services to improve the overall well-being and quality of life of WLHIV (22,54). Understanding how menopause is experienced by WLHIV in SSA is crucial to guide healthcare interventions, inform policy, and address gaps in HIV and women's health research.

1.2 Aims

The existing body of research on menopausal experiences among WLHIV in Sub-Saharan Africa lacks comprehensive evaluation in published studies. This scoping review aims to explore the existing literature on menopause among women living with HIV in Sub-Saharan Africa to guide healthcare interventions, inform policy, and shape future research.

Objectives:

The primary objective of this scoping review is to provide a comprehensive overview of the literature on menopause among women living with HIV compared to women living without HIV in Sub-Saharan Africa.

The secondary objective of this scoping review is to identify knowledge gaps and key themes in current literature that address menopause among women living with HIV compared to women living without HIV in Sub-Saharan Africa.

1.3 Research question

Our main research question, "What is the current body of research and state of knowledge on the experience of menopause among women living with HIV in Sub-Saharan Africa?" was formulated using the PCC (Population, Concept, Context) framework and adheres to the Joanna Briggs Institute (JBI) guidelines for conducting scoping reviews and formulating scoping review questions (55).

The scope of this review study was established through consideration of the following relevant research questions stated below:

1. How do women living with HIV experience menopause compared to women living without HIV in Sub-Saharan Africa, and how do these experiences compare globally?
2. What are the prevalent menopausal symptoms experienced by women living with HIV compared to women living without HIV?
3. What are the existing gaps in the literature regarding menopause experiences in women living with HIV in Sub-Saharan Africa, and what areas require further research and exploration?
4. How is menopause defined in studies and how are menopausal symptoms measured in WLHIV?
5. What methodological approaches are used in existing studies to address the menopause experiences among WLHIV in Sub-Saharan Africa?

2. Methods

Our scoping review adhered to guidelines outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR), shown in [Appendix V: PRISMA 2020 checklist](#) (56). The methodology applied was based on that of JBI for scoping reviews (57). The steps of the framework we employed for our scoping study are as follows: (i) formulating the research question, (ii) identifying relevant studies, (iii) study selection, (iv) collating and analysing data, (v) synthesising and presenting findings (58,59).

2.1 Data sources

Online Databases PubMed, Science Direct and Google Scholar were used to conduct a literature search by the primary reviewer (author) to identify potential research articles published up to October 2023. Additionally, we also screened the reference lists of potential studies for further relevant articles.

2.2 Search strategy

The following search strategy was used for the study according to the JBI PCC framework (57). The search strategy was built on three key concepts: (i) Menopause (ii) HIV (iii) Sub-Saharan Africa, along with related search terms to ensure the inclusion of potential articles. Search strategies focused on keywords such as “HIV”, “menopause” and “Sub-Saharan Africa”. The keywords were expanded with synonyms and combinations using Medical Subject Headings (MeSH) to identify all relevant articles. Boolean operators (AND/OR) and truncations (“”, *) were also included. [Appendix III](#) provides a detailed list of search terms and keywords. An initial pilot search was conducted in September 2023, and most searches were conducted in October 2023. Originally developed for PubMed, the search was modified for each additional database. Keywords that did not generate relevant search results were removed, and the search strategy was adjusted, as necessary. The primary reviewer (author) drafted the search strategy using these keywords with guidance from the supervisor. In addition, an experienced senior librarian reviewed the search strategies to ensure the most effective keyword selection and search strategy for each database. Finally, the supervisor reviewed the final strategies. [Appendix II](#) outlines the search strategies for each database.

2.3 Eligibility criteria

We aimed to include research that will improve our knowledge of the menopause experiences of WLHIV in Sub-Saharan Africa. Only original peer-reviewed studies developed within an empirical framework were included to ensure the quality of the selected studies. Our search was limited to studies published in English. Although no study publication time restrictions applied, studies published within the past decade were prioritised to ensure quality and relevance.

Eligible research designs included observational studies i.e. cohort, longitudinal, case-control, case series, and cross-sectional studies. Scoping reviews, systematic reviews, meta-analyses, editorials, commentaries, guidelines, care recommendations, websites and book sections, encyclopaedia, conference abstracts, book reviews, discussions or communications and all studies without original data were excluded. We considered relevant studies in scoping and systematic reviews that met our inclusion criteria and identified any studies that were missed in our initial search. Studies not meeting our eligibility criteria were still considered in the overall context of our literature review. Exclusion criteria were determined by the studies' ability to provide relevant data to address review questions.

2.3.1 Population

Inclusion criteria involved studies on perimenopausal and postmenopausal women aged ≥ 40 years living with HIV in Sub-Saharan Africa. Exclusion criteria involved pre-menopausal women, women without HIV, non-menopausal women, pregnant women, women aged < 40 years, breastfeeding women, and those who had undergone hysterectomy. Perimenopausal women were defined

according to WHO and STRAW+10 criteria as those experiencing menstrual irregularity or hormonal changes prior leading up to menopause, while postmenopausal women were defined as those with 12 months of amenorrhoea after the final menstrual cycle not due to other causes (9,10).

2.3.2 Concept

All relevant studies on menopause experiences among women living with HIV in Sub-Saharan Africa were included. Studies focused on menopause and HIV in Sub-Saharan Africa were excluded.

2.3.3 Context

Studies included those conducted in the Sub-Saharan Africa region. Any studies focused on regions outside of Sub-Saharan Africa were excluded.

Table 1: Inclusion and exclusion criteria for studies in our review

Criteria	Inclusion	Exclusion
Population	Perimenopausal and postmenopausal women living with HIV	Premenopausal women, women living without HIV, non-menopausal women, men, pregnant women, women aged < 40 years, breastfeeding women, and women who have undergone hysterectomy
Concept	Menopause, menopause symptoms, menopause-related comorbidities	Outcomes, comorbidities, and symptoms unrelated to menopause
Context	Sub-Saharan Africa	Europe, the United States, North America, Asia
Type of Study	Original peer-reviewed research articles Quantitative studies, empirical research, observational studies, i.e. cohort, longitudinal, case-control, case series, and cross-sectional studies	Non-peer-reviewed research articles Qualitative studies, mixed-method studies Scoping reviews, systematic reviews, meta-analyses, commentaries, guidelines, care recommendations, editorials, websites, book sections, encyclopaedias, conference abstracts, book reviews, discussions, communications, case reports, theses, and conference papers.
Time of publication	No restrictions	None
Language	English	Any other language other than English

2.4 Study selection

Our scoping review follows the recommendations from the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (60). The PRISMA Extension for Scoping Reviews (PRISMA-ScR) guidelines were followed in conducting this scoping review (57). The final search results were exported into Covidence online screening tool software for eligibility. Duplicates were removed both manually and through Covidence. Titles of relevant articles were identified for inclusion in our scoping review according to our eligibility criteria. Abstracts were then screened for relevance, followed by full-text reviews of the selected papers. This review process followed an iterative approach in accordance with the scoping review methodology (58). Articles were excluded if they did not meet our eligibility criteria or were not relevant to our topic of interest. Covidence improved

screening efficiency by identifying duplicates and documenting reasons for the inclusion and exclusion of articles. The primary reviewer (author) performed the study selection for relevant articles and verified in consultation with the supervisor to reduce bias. Although dual independent screening and selection were not feasible, any discrepancies with the supervisor were resolved through discussion.

2.5 Quality Assessment

Our review did not include a critical appraisal or risk of bias assessment, as the methodological quality of the included studies was not evaluated, following scoping review criteria (57).

2.6 Data extraction

Data extraction occurred from October to November 2023. Extracted data from articles included: author(s), title, year of publication, study location, objectives/aim, study design, study population, sample size, measure(s), measurement tools, menopause definitions, outcome(s) and main findings that relate to the scoping review research questions, where applicable. A data extraction form was designed in Excel (61) in accordance with the JBI Manual for Evidence Synthesis (62). Extracted data were summarised in tabular format (see [Appendix VI](#)). The main reviewer used Covidence software to gather information from eligible studies. The data was examined in an iterative process, with inconsistencies checked and addressed by the reviewer. Data was double-checked to ensure accuracy. Any missing information regarding any of the above was not included.

2.7 Data synthesis and analysis

Studies were grouped by themes in accordance with the review objectives and research question(s). Key themes identified included: early menopause, menopausal transition, menopause symptoms, bone health, and obesity. All relevant information and characteristics from the included studies were summarised by study location, sample size, year of publication, methods, study design, and measures used. A comprehensive summary of the characteristics of each study included in our review is presented in [Appendix VI](#).

3. Results

Literature search results

Our initial database search identified a total of 156 potential articles from the selected databases. Of these, 84 were from PubMed and 18 from Science Direct, while an additional 44 articles were identified through Google Scholar. After importing the 138 eligible studies onto the Covidence software tool used for screening, 17 duplicates were removed, and one duplicate was identified manually. 138 studies were screened by title and abstract, and 66 were excluded. Full-text eligibility

of 72 studies was then assessed, and 65 were excluded. The primary reasons for article exclusion were that 46 articles had the wrong patient population, 13 had the wrong outcomes, and 6 had the wrong study design. Seven studies were included in the final review. An overview of the study selection and exclusion process is presented in **Figure 1** (see also **Appendix IV**).

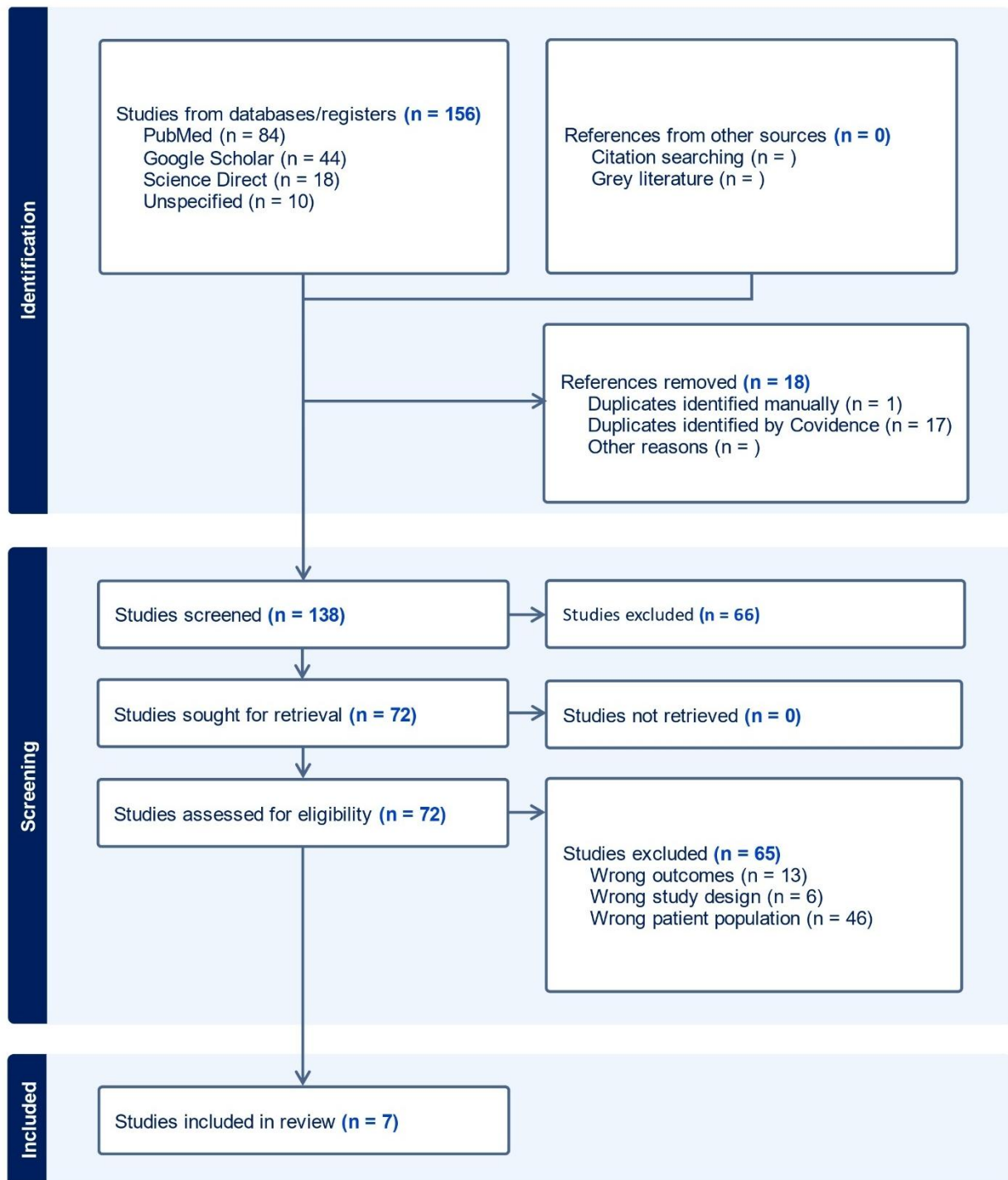


Figure 1: PRISMA Flow chart outlining the study selection and exclusion process for our scoping review (57).

Characteristics of included studies

In our scoping review, a total of seven studies were included, published between 2014 and 2023. The majority of these studies ($n=4$, 57.1%) were published between 2021 and 2023. Most studies were conducted in South Africa, followed by Nigeria ($n=4$, 28.6%) and Zimbabwe ($n=1$, 14.3 %). The majority of studies were conducted in upper-middle-income countries (UMICs) ($n=4$, 57.1%), while the remaining studies were from low and lower-middle-income countries (LMICs) ($n=3$, 42.9%). In terms of study design, most studies were cross-sectional ($n=5$, 71.4%), with sample sizes ranging from 378 to 714 participants. Two studies ($n=2$, 28.6%) were longitudinal cohort studies, with sample sizes ranging from 120 to 504 participants. A summary of study characteristics is provided in [Appendix VI](#).

Measurement Tools

The Menopausal Rating Scale (MRS) was the most commonly used tool in studies to determine menopause status, identify menopause symptoms, menopausal transition (MT) stage, and vasomotor symptoms (VMS) severity ($n=5$, 27.8%). Other tools include the brief version of the World Health Organization's Quality of Life instrument (WHOQoL-BREF) questionnaire, which measures the quality of life in four dimensions (i.e. physical, psychological, social, and environmental) ($n=4$, 22.2%), the Global Physical Activity Questionnaire (GPAQ) to quantify self-reported physical activity ($n=4$, 22.2%), Dual-energy X-ray absorptiometry (DXA) to determine body composition and bone mineral density (BMD) ($n=2$, 11.1%), Shona symptom 14 item questionnaire to assess mental health ($n=2$, 11.1%), and the Stages of Reproductive Aging Workshop (STRAW +10) Criteria to categorize women into different menopause stages ($n=1$, 5.6%) (63).

Menopause definitions

The scoping review identified a range of criteria used to define menopause among women living with HIV in Sub-Saharan Africa. Out of the seven included studies, only one study defined natural menopause. The primary definition of menopause used was the absence of menstruation for ≥ 12 consecutive months, following WHO guidelines (64,65). Pre-menopause, perimenopause, and postmenopause were consistently defined in all seven included studies. Classification often relied on the current menstrual status of participants, while other studies used the duration of amenorrhea. Although the criteria for classification varied from considering menstrual patterns to self-reported last menstrual period (LMP) (66). It is important to note that age thresholds were established to define early menopause as occurring at or below 45 years of age (65). [Table 2](#) presents the definitions of menopause used across the included studies.

Table 2: Menopause definitions described by authors in the scoping review

Author(s)	Premenopausal	Perimenopausal	Postmenopausal	Additional definitions
<i>Agaba et al. 2017 (67)</i>	Women with regular menstrual cycles	Absence of menses in at least three cycles, but no more than 11 during the past 12 months	Amenorrhea for 12 months or more	Age at natural menopause ≤ 45 years
<i>Agaba et al. 2017 (65)</i>	Women with regular menstrual cycles	Absence of menses in at least three cycles, but no more than 11 during the past 12 months	Amenorrhea for 12 months or more	Natural menopause: Permanent cessation of menstruation after 12 months without menstruation. Early menopause: Natural onset of menopause at ≤ 45 years of age.
<i>Madanhire et al. 2023 (68)</i>	Women currently experiencing regular periods	Women experiencing irregular periods	Women who had not been bleeding for more than a year	None
<i>Madanhire et al. 2023 (28)</i>	Women currently experiencing regular menstruation	Women who had irregular periods or experienced three consecutive months of missed menstruation in the past year	Women who had not experienced menstruation for a year	None
<i>O Breasail et al. 2022 (66)</i>	Women currently having regular periods	Women having irregular periods	Women who had amenorrhea for >12 months	Categorised into menopausal groups according to their self-reported last menstrual period (LMP)

Included studies and key themes

The key themes identified in the studies included early menopause, menopausal symptoms, the menopausal transition, obesity, and bone health. A comprehensive summary of the seven studies included in our review is presented in tabular format (see [Table 6](#) included in [Appendix VI](#)) outlining the key characteristics. Furthermore, several of these identified themes overlapped, with many topics appearing in individual studies.

Early menopause

Early menopause (EM) prevalence and its associated factors were determined by a cross-sectional study conducted on 714 women aged 40 years and above in Jos, North Central Nigeria (65). The outcome measure was age at natural menopause ≤ 45 years. It was found that early menopause was common in the cohort of HIV-infected women in Nigeria, and was associated with HIV infection, early menarche, and sexual activity. Among the women studied, the prevalence of early menopause was 22.9% (95% CI 17.9–28.6%), with an average age of 43 years. The findings showed that EM was significantly more prevalent in HIV-positive women compared to HIV-negative women (27.9% [95% CI: 1.22–34.2%] vs 2.7% [95% CI: 0.1–14.2%], $p < 0.001$). Women experiencing early

menopause were younger ($p < 0.001$) and had a shorter duration of HIV infection ($p = 0.007$). More than 25% of postmenopausal women reported experiencing early menopause. Early menopause was independently associated with early menarche (AOR: 14.88, 95% CI: 1.37–161.10) and sexual activity (AOR: 2.02, 95% CI: 1.03–3.96). Additionally, HIV infection (AOR: 10.95, 95% CI: 1.39–86.33) and sexual activity (AOR: 2.37, 95% CI: 1.24–4.52) were associated with EM across all participants. Baseline CD4+ cell count ($p = 0.66$) and viral load ($p = 0.15$) were comparable between those with and without early menopause (65). However, no HIV-related factors were found to be predictors of EM, suggesting that the relationship between HIV infection and early menopause is likely complex and influenced by multiple factors, including unemployment, younger age, shorter duration of HIV diagnosis, co-infection with hepatitis C virus, and a shorter duration of highly active antiretroviral therapy (HAART). There was no significant association identified between HIV-related factors and early menopause.

Menopausal transition

Two studies reported menopausal transition in our scoping review. One cross-sectional study found a higher age at final menstrual period (FMP) in women within 4 years of FMP compared to those 10 years or more after FMP (63). Lower body mass index ($< 25 \text{ kg/m}^2$) was associated with an earlier age at FMP compared to women in higher BMI groups. Age at FMP was similar for women in menopause stages occurring immediately before and after the FMP. The study used the STRAW + 10 criteria to assess the age at FMP among women in different menopausal stages while exploring the impact of ageing on menopausal symptoms, hormone levels, and BMI (63). A cohort study on 504 black South African women aged 40–60 years transitioning through menopause found significant declines in BMD across all skeletal sites. Transitioning from pre- to post-menopause was associated with greater total body BMD losses in WLHIV compared to those without HIV (68).

Menopausal symptoms

Three studies compared the prevalence and severity of menopausal symptoms in WLHIV in Sub-Saharan Africa using the Menopause Rating Scale (MRS). Across the included studies, WLHIV reported a wide range of menopausal symptoms across vasomotor, somatic, psychological, and urogenital domains compared to their HIV-negative counterparts. A cross-sectional study on 714 WLHIV between the ages of 40–80 years in Jos, Nigeria compared the prevalence of menopause symptoms between WLHIV to their HIV-negative counterparts, and identified predictors of severe menopause symptoms and associated factors (67). The most prevalent menopause symptoms included hot flushes (67.2%), joint and muscle discomfort (66.2%), physical and mental exhaustion (65.3%), heart discomfort (60.4%), and anxiety (56.4%). WLHIV experienced more severe symptoms than their negative counterparts, with a median MRS score significantly higher for HIV-positive women ($p=0.01$). WLHIV showed greater severity scores in the psychological and somato-

vegetative domains of menopausal symptoms, potentially influenced by lifestyle factors such as smoking. Both HIV status and a history of cigarette smoking were identified as independent predictors of severe symptoms. Factors associated with severe menopause symptoms included being HIV-positive (AOR: 3.01, 95% CI 1.20–7.54) and a history of cigarette smoking (AOR: 4.18, 95% CI 1.31–13.26). The study also found that being married (AOR: 0.49, 95% CI: 0.32–0.77), premenopausal (AOR: 0.60, 95% CI: 0.39–0.94), and having a good quality of life (AOR: 0.62, 95% CI: 0.39–0.98) were protective factors against severe menopause symptoms, leading to decreased symptom severity. The severity of symptoms was associated with the stage of menopausal transition, with premenopausal women having a 40% lower likelihood of experiencing severe symptoms compared to peri/postmenopausal women. Being married was associated with a reduced risk of severe symptoms, while the stage of menopausal transition was significantly associated with increased symptom severity, particularly among unmarried women (i.e. separated, divorced, widowed, or single), who had a higher probability of experiencing severe menopausal symptoms (67).

A cross-sectional study conducted on 378 WLHIV aged 40–60 years in Harare, Zimbabwe (28) assessed the prevalence and severity of self-reported menopause symptoms across various stages of the menopausal transition, while examining potential factors associated with these symptoms. The findings indicated that WLHIV may experience more intense menopausal symptoms compared to women without HIV. A higher prevalence of moderate (24.9% vs. 18.1%) and severe (9.7% vs. 2.6%) menopausal symptoms, particularly in the somatic and psychological domains, was reported among WLHIV compared to their negative counterparts. Furthermore, the stage of menopause was significantly associated with the occurrence of these symptoms. HIV infection was associated with more severe menopause symptoms (OR: 2.02 [95% CI 1.28, 3.21]), along with other contributing factors such as unemployment (OR: 1.56 [0.99, 2.46]), alcohol consumption (OR: 2.16 [1.01, 4.62]), food insecurity (OR: 1.93 [1.14, 3.26]), mood disorders (OR 8.80 [2.77, 28.0]), ≥ 2 falls per year (OR: 4.29 [1.18, 15.6]) and early menarche (OR: 2.33 [1.22, 4.48]) (28).

The study also found that 25.4% of women with HIV reported moderate or severe psychological symptoms, and 46.5% had moderate or severe urogenital symptoms. Peri-menopausal WLHIV had higher MRS scores than those pre- and post-menopausal women, while menopausal stage did not affect MRS scores in HIV-negative women ($p=0.014$). Menopausal symptoms significantly impacted health-related quality of life (HRQoL), with WLHIV experiencing moderate to severe symptoms reporting lower HRQoL than those without symptoms. In WLHIV, moderate and severe psychological and urogenital symptoms were associated with lower HRQoL. Notably, as the severity and frequency of menopausal symptoms increased, mean lower HRQoL scores decreased. HIV infection did not appear to modify the relationship between menopausal symptoms and HRQoL. Hypertension was found in 31.6% of women, but less common among those living with HIV. Peri-menopausal WLHIV

reported the highest frequency of symptoms, with 78% experiencing somatic or urogenital, and 69% psychological symptoms. Pre-menopausal women with HIV also had a high prevalence of psychological symptoms (57%). Overall, the findings suggest that HIV infection leads to more severe somatic and psychological symptoms during menopause (28).

A cross-sectional study involving 702 HIV-positive and HIV-negative women aged 40-60 years in South Africa found no significant differences in the prevalence of menopausal symptoms between the two groups (63). The presence of menopausal symptoms was not influenced by HIV status. The research also indicated that the prevalence of vasomotor symptoms and sexual issues significantly increased during early post-menopause compared to the late reproductive stage ($p < 0.05$). Irritability was more common in the late post-menopause phase, as women in the late postmenopausal phase were at a significantly higher risk of increased irritability ($p < 0.05$). Furthermore, a higher BMI was associated with a greater prevalence of irritability. No significant trends were observed for other menopausal symptoms across the various stages of menopause (63). These findings are summarised in [Table 3](#).

Table 3: Menopause symptom prevalence and severity among WLHIV vs WLWOH in SSA

Author(s)	Measurement Tool(s)	Key Symptoms Reported	Prevalence & Severity (WLHIV vs WLWOH)	Main Findings
<i>Agaba et al. (2017, Nigeria) (67)</i>	Menopause Rating Scale (MRS); Self-reported 12-month amenorrhoea	Hot flushes (67.2%), joint/muscle pain (66.2%), exhaustion (65.3%), heart discomfort (60.4%), anxiety (56.4%)	Significantly higher median MRS score ($p=0.01$); greater severity in psychological & somatic domains Lower symptom severity overall	HIV+ (AOR 3.01, 95% CI 1.20–7.54) and smoking (AOR 4.18, 95% CI 1.31–13.26) predicted severe symptoms; being married & premenopausal were protective
<i>Madanhire et al. (2023, Zimbabwe) (69)</i>	Menopause Rating Scale (MRS)	Somatic, psychological (25.4%), and urogenital (46.5%) symptoms	Moderate (24.9% vs 18.1%) and severe (9.7% vs 2.6%) symptoms; WLHIV had higher MRS scores	WLHIV had more intense symptoms (OR 2.02, 95% CI 1.28–3.21); symptoms worsened HRQoL ($p<0.05$); peri-menopausal WLHIV most affected
<i>Jaff et al. (2014, South Africa) (63)</i>	STRAW+10 stages; self-report	Vasomotor symptoms, irritability, sexual dysfunction	No significant differences in overall symptom prevalence between the two groups	HIV status not associated with menopausal symptom presence; vasomotor and sexual symptoms increased in early postmenopause ($p<0.05$); BMI increase correlated with irritability

Bone health

Three studies reported on the association between HIV and menopause on bone health using dual-energy X-ray absorptiometry (DXA) in WLHIV compared to WLWOH. In a cohort study of 504 urban-dwelling South African women aged 40–60 (68). Postmenopausal WLHIV experienced significantly greater total body BMD loss (OR: 0.070 [0.031, 0.108]; $p=0.001$) compared to postmenopausal women without HIV (OR: 0.036 [0.015, 0.057]; $p=0.049$). This difference was particularly evident at the total body (TB) and lumbar spine (LS) sites. The transition from pre- to postmenopause was associated with greater total body BMD losses in women with HIV (OR: 0.092 [0.042, 0.142] g/cm²; $p=0.001$) compared to those without HIV (OR: 0.038 [0.016, 0.060] g/cm²; $p=0.034$). Postmenopausal WLHIV experienced significant declines in the lumbar spine and total hip BMD, with a 9.0% loss in lumbar spine BMD and a 4.5% loss in total hip BMD compared to pre-or perimenopausal women, indicating a significant decline in BMD with menopausal progression (68).

A smaller cohort study involving 120 postmenopausal South African WLHIV aged over 45 years on ART also used the DXA tool to identify factors associated with changes in BMD (70). This study found that bone mineral density was significantly associated with factors such as body weight, duration of HIV infection, and BMI. Postmenopausal HIV-infected women were suggested to experience a gradual reduction in bone density, influenced by factors like calcium intake, serum vitamin D concentration, and physical activity level. Factors such as time, age, and physical activity (PA) are also associated with BMD, with age and physical activity showing a positive correlation with left femoral neck (LFN) BMD ($p = 0.008$). Over a two-year follow-up period, 8.3% of the women reported experiencing fragility fractures. Although there was a slight, yet statistically significant increase in total BMD, the effect size was small. Additionally, the study found that serum parathyroid hormone (PTH) levels increased inversely with a significant decrease in serum 25-hydroxyvitamin D (25(OH)D), confirming the previously reported inverse relationship between vitamin D and PTH (71).

A cross-sectional study of 430 Black African women aged 40–60 years examined the impact of HIV status on the relationship between menopause and bone health outcomes (66). The findings revealed that menopause is associated with reduced bone density and strength at the distal radius, a common site of osteoporotic fractures. Deficits in cortical volumetric bone mineral density (vBMD), as well as lower cortical density and thickness at the proximal radius, were also observed. Both WLHIV and HIV-negative women exhibited similar patterns of decreased radial total vBMD and bone strength index (BSIc) across menopause stages, although this trend was more pronounced in HIV-negative women, likely due to a smaller sample size of women living with HIV. Later stages of menopause were associated with significantly lower total mean vBMD (premenopause: 345.7 [335.8, 355.5] vs. postmenopause: 330.1 [322.7, 337.6] mg/cm³, $p= 0.017$) and BSIc (premenopause: 0.39 [0.37, 0.41] vs. postmenopause: 0.36 [0.35, 0.37] g²/cm⁴; $p=0.012$), with women showing lower total BMD at the distal radius compared to those in earlier menopausal stages.

Obesity

Limited evidence was found on the association between obesity and menopause in women living with HIV in Sub-Saharan Africa. A cross-sectional study conducted on 702 urban Sub-Saharan African women examined reproductive ageing to assess the impact of obesity on the menopausal transition (MT), FMP, and menopausal symptoms (63). The study used STRAW + 10 criteria to categorise women into different menopause stages and used the MRS tool to assess symptoms, menopause status, VMS severity, MT Stage, and FSH levels. Obesity was found to be strongly associated with a higher risk for severe VMS, with a prevalence of 28% in the BMI group of ≥ 35.0 kg/m² compared to those with lower BMI. Furthermore, obesity was significantly associated with age at FMP ($p = 0.0007$), suggesting a relationship between obesity and menopause timing. Higher BMI (BMI ≥ 35.0 kg/m²) was also associated with a greater prevalence of irritability, sleep disturbances, and joint problems. Women with lower BMI (< 25 kg/m²) experienced an earlier age at FMP compared to those with higher BMI levels. Additionally, a prospective study published in 2021 found significant associations between BMI and body weight with BMD in WLHIV in South Africa (70).

4. Discussion:

Summary of findings

This scoping review identified seven primary studies exploring the menopausal experiences of women living with HIV (WLHIV) in Sub-Saharan Africa (SSA), highlighting the complex relationship between menopause and HIV. The findings suggest that WLHIV experience more severe menopausal symptoms (vasomotor, urogenital, psychological, and somatic symptoms were commonly reported), an earlier onset of menopause, and lower bone mineral density compared to women without HIV in SSA. However, the evidence across studies was inconsistent, partly due to variations in study design, definitions of menopause and measurement tools. Several studies were excluded during the full-text screening and evaluation of study eligibility due to the wrong patient populations or outcomes. The majority of eligible studies included in our review were conducted in South Africa, Nigeria, and Zimbabwe. While these countries are key regions in Sub-Saharan Africa, the concentration of research in these specific areas limited the generalizability of our findings. Additionally, most of the included studies were cross-sectional, highlighting the lack of longitudinal prospective cohort studies in this field.

Methodology

Studies defined menopause according to the WHO definition, which is widely recognised and employed in most literature (72). Although few variations were observed across studies, most definitions were similar. The included studies used WHO or STRAW+10 definitions, ensuring international comparability. Both the STRAW+10 and WHO classifications of menopause and its

stages are commonly referenced in academia (51). The most commonly used measurement tool in our review was the MRS tool, a widely recognised tool for assessing menopausal symptoms (63). While there was some variability in the scales used to assess symptom severity (e.g., no or little, mild, moderate, severe, very severe), a consistent approach was observed in categorising symptoms into somatic, psychological, and urogenital sub-domains. However, not all tools address all relevant symptoms, and they may not adequately account for cultural differences in symptom prevalence and severity (73–75). It is important to consider cultural factors when documenting menopausal symptoms in women living with HIV (76). Although the MRS tool has been translated into various languages and used globally (74), there are currently no menopause rating tools specifically designed for women living with HIV from diverse cultural backgrounds (51,77). The MRS was originally developed for populations in Europe, North America, Latin America, and Asia, and has not been specifically validated for women living with HIV (78). Although it is widely used in North America (21,79), its application has been less common in Sub-Saharan Africa (25). None of the included studies adapted instruments to local languages or cultural contexts, limiting comparability and external validity. It is important to consider the assessment methods for menopausal symptoms, as research indicates that women living with HIV may find it difficult to distinguish between symptoms related to menopause and those associated with HIV and ART (12,21,80). The overlap between HIV-related and menopausal symptoms may result in misdiagnosis or under-management of menopause in HIV care. Finally, most studies on menopause have excluded significant subgroups, such as women who had undergone hysterectomy, and lacked qualitative components that could better capture the lived experience of menopause. These methodological gaps constrain understanding of the full spectrum of menopausal health among WLHIV in SSA.

Early menopause

Early menopause emerged as a significant concern among women living with HIV, with many studies indicating a higher prevalence of early menopause compared to HIV-negative women. A study in Nigeria found a high prevalence of early menopause (22.9%) among HIV-positive women, with a mean age of 43 years (65). Although the study did not identify any HIV-related factor predicting early menopause, the relationship between HIV infection and early menopause is likely complex and influenced by other factors. Previous research suggests that HIV may contribute to an earlier onset of menopause due to chronic inflammation, premature ovarian insufficiency, and opportunistic infections (35). Studies in Canada and Brazil have shown a high prevalence of early natural menopause, with 16.6% to 27% of women experiencing menopause at a younger age (81). A prospective cohort study in Brazil revealed a high prevalence of early natural menopause, with 27% of women experiencing menopause at a younger age (42). Furthermore, the longitudinal, multi-ethnic Study of Women's Health Across the Nation (SWAN) involving middle-aged women in the US highlighted significant differences in the onset of perimenopause between women of Hispanic

ethnicity and those of Caucasian, African American, Chinese, and Japanese backgrounds, with Hispanic women experiencing perimenopause two years earlier than women from other ethnic groups (82). However, data on age at menopause in women living with HIV have been conflicting. Some studies suggest that WLHIV experience menopause at an earlier age compared to HIV-negative women (19,36,52), while other studies have found no significant association between HIV and earlier menopause (83,84). Previous studies have reported the median age of menopause in WLHIV is 50 years (34), which is similar to the median age of menopause of 51.4 years reported in African American women participating in the SWAN study (85). However, the findings are inconsistent. Another study found that African American WLHIV have a median age of menopause of 49 years (86), similar to findings in women from France (36). A retrospective analysis of a Swiss HIV cohort study revealed a median menopause age of 50 years, approximately two years earlier than that reported for HIV-negative women, with early menopause being significantly associated with Black ethnicity (52.2% vs. 21.6%, $p < 0.001$) (35). Research has shown that ethnicity influences menopause age, with women of Black ethnicity being four times more likely to experience early menopause compared to women of other ethnicities (35,87). Multiple cross-sectional studies involving women living with HIV have reported a lower median age at menopause, with various studies reporting a much lower median age at menopause of 46 years in a US cohort (88), 47 years in Thailand (19), 48 years in a Spanish multicentre cohort (27) and prospective cohort and cross-sectional studies in Brazil (42,89), consistent with findings from two studies in Nigeria and Ghana respectively (24,90). A prospective study on women aged 35 – 59 years found that WLHIV were 73% more likely to experience premature menopause compared to HIV-uninfected women (38). Furthermore, an earlier menopause age in WLHIV may increase the risk for osteopenia (91) and susceptibility to osteoporosis (92).

Bone Health

Our review suggests that the association between HIV and menopause has significant implications for bone health in women living with HIV. These findings are consistent with existing literature, as multiple studies included in the review reported that WLHIV experience higher BMD loss and an increased risk of fractures compared to HIV-negative women (66,70). Across various stages of menopause, WLHIV consistently show lower bone density and bone strength, suggesting that HIV may exacerbate the effect of menopause-related bone loss (66). Research has indicated that HIV is independently associated with decreased BMD (8,93), with postmenopausal WLHIV experiencing accelerated bone resorption and significantly lower BMD (70). Furthermore, WLHIV transitioning through menopause show accelerated bone loss, particularly at the total body and lumbar spine sites, compared to women without HIV (68). A study in the United States found that WLHIV had a 5–9% lower areal BMD at various skeletal sites compared to HIV-negative women (8). This rapid bone loss is a potential risk factor for osteoporotic fractures, as observed in WLHIV in South Africa

(94). Previous studies have reported an increased probability of low BMD (95,96), greater bone loss (97) and higher fracture risk (98) among postmenopausal WLHIV compared to premenopausal women. Postmenopausal status has been consistently associated with lower BMD (95,97,99–102), highlighting the combined effects of menopause and HIV on bone health. A multinational study involving diverse populations, including Australia, Belgium, Brazil, India, Ireland, Peru, Spain, Thailand, the USA, the UK, and South Africa, reported a high prevalence of low BMD at 35.1% among individuals with HIV(103). Similar findings have been observed in other studies, which reported a higher prevalence of low BMD in women with HIV (27%) compared to those without (19%) (93). Low BMD was also indicated in a cross-sectional study conducted on middle-aged women with HIV (93). Additionally, a multiracial study found that HIV was significantly associated with BMD loss in non-Black women (93), while Black women experienced a greater decline in BMD related to menopause (104). Both menopause and HIV are recognised as significant risk factors for osteoporosis (35), with Black women facing a higher risk (104). However, regardless of the substantial evidence associating HIV with decreased BMD, most studies on bone health and HIV have been conducted in Europe and North America, with limited research in Sub-Saharan Africa (8). Therefore, generalisations from Western populations may not be applicable to the Sub-Saharan African context.

Obesity

Although limited evidence was found on the association between obesity and menopause among WLHIV in Sub-Saharan Africa in our review, the few included studies indicated a significant association between obesity and menopausal experiences among WLHIV (63,70). Obesity was strongly associated with a higher risk of symptom severity, with women in higher BMI groups (≥ 35.0 kg/m²) reporting a significantly greater prevalence (28%) of severe or very severe vasomotor symptoms compared to those in lower BMI groups (63). Additionally, postmenopausal HIV-infected women have shown a significant association between BMI and bone health outcomes (70). Despite these findings, evidence remains inconsistent. A cross-sectional analysis involving 396 women aged 45–60 years receiving care at HIV clinics in England found no association between menopausal status and obesity (105). Furthermore, research conducted in Western societies has shown varying results, with some studies indicating a significant association between higher BMI and the severity of menopausal symptoms. Current literature suggests that higher BMI, waist circumference, and waist-to-hip ratio are associated with more severe menopausal symptoms, including hot flashes and night sweats (106). However, the influence of obesity on menopausal symptoms may differ with age, while a higher BMI is significantly associated with increased hot flashes during the menopausal transition, is correlated with a reduced risk in the postmenopausal period (107). Overall, limited research on the association between obesity and the prevalence of vasomotor symptoms remains in this population (63).

Menopausal Transition:

Studies have explored stages of menopausal transition, and the factors associated with them (63,68), revealing that age at the final menstrual period (FMP) varies among women in different menopausal stages (63). However, it was found that the reported age at FMP among Black urban South African women interviewed four years or more after their FMP was unreliable, highlighting the importance of timely data collection for accurately assessing age at FMP, and minimising recall bias. In postmenopausal black South African WLHIV, the menopausal transition is associated with declines in BMD and increased fat mass, leading to a higher risk of osteoporotic fractures and metabolic complications (28). Although the STRAW + 10 criteria are recognized as a valid measure of reproductive ageing (63) and are commonly used to categorize women into menopause stages, their terminology may not be easily applicable to women in rural and informal urban settings in resource-limited countries (108). Previous studies in sub-Saharan Africa have not applied the STRAW + 10 recommendations for staging menopausal transition (63). Therefore, additional research is required to understand the experiences of menopause among WLHIV in Sub-Saharan Africa and how these experiences compare to those in other global contexts.

Menopausal symptoms

Our review revealed a higher prevalence of moderate to severe menopausal symptoms among WLHIV in Sub-Saharan Africa compared to their HIV-negative counterparts, including an increase in somatic symptoms (such as hot flushes, cardiac issues, and joint and muscle discomfort) and psychological symptoms (including mood disorders, anxiety, and mental exhaustion), as well as early menarche (63,67,68), consistent with findings from other studies (11,27,39,80,83). In Nigeria, WLHIV reported significantly more severe menopausal symptoms than HIV-negative women (67). Independent predictors of severe menopausal symptoms included HIV status and a history of cigarette smoking. HIV-positive status (AOR: 3.01, 95% CI: 1.20–7.54) and smoking history (AOR: 4.18, 95% CI: 1.31–13.26) were significantly associated with severe symptoms, aligning with previous studies reporting an association between smoking and a higher risk of somatic symptoms (27,29). Protective factors against severe menopausal symptoms included being married, premenopausal, and having a good quality of life, while unmarried individuals were more likely to experience severe symptoms (67). The severity of symptoms was also associated with the stage of menopausal transition (67), with premenopausal women having a 40% lower likelihood of experiencing severe symptoms, similar to findings from a multicentre Spanish cohort study, where 45.5% of premenopausal women reported menopausal symptoms (27).

Furthermore, peri- and postmenopausal stages were associated with a higher likelihood of somatic symptoms (AOR 3.01; 95% CI 1.38 – 6.55 and AOR 2.63; 95% CI 1.44-4.81, respectively), while postmenopause significantly increased the likelihood of psychological (AOR 2.16; 95% CI 1.13-4.14)

and urogenital symptoms (AOR 2.54; 95% CI 1.42–4.85). Postmenopausal women exhibited a five-fold increase in the likelihood of severe urogenital symptoms compared to premenopausal women (AOR 4.90; CI 1.74–13.84). Additionally, postmenopausal women had a significant five-fold increase in the likelihood of severe urogenital symptoms compared to pre-menopausal women (AOR 4.90; CI 1.74–13.84). However, no significant differences were found in menopausal status concerning anxiety or depression. The most frequently reported symptoms across all women included joint and muscle issues, exhaustion, and sleep disturbances. Notable differences in the prevalence of vaginal dryness ($p=0.002$), joint or muscle complaints ($p=0.032$), and sweating or flushes ($p=0.032$) were observed among the three groups. Vasomotor symptoms, such as hot flushes and night sweats, were particularly prevalent during menopause (18,109). A retrospective review indicated that vasomotor symptoms were the most common, affecting 84% of participants, followed by menstrual cycle changes at 62% (83). Over half of the patients (56%) reported psychological symptoms, including mood changes, depression, anxiety, irritability, and fatigue, while 29% experienced urogenital symptoms, such as vaginal dryness and urinary tract issues.

In Thailand, postmenopausal women living with HIV reported more vasomotor symptoms (19), and similar patterns were observed in Brazil, where 97.9% of HIV-infected women experienced psychological symptoms and 78.1% reported vasomotor symptoms (20). A study on African American women found a high prevalence (80%) of hot flashes among HIV-infected women, compared to 38-69% in the general population (34). WLHIV in Zimbabwe exhibited distinct patterns of symptom severity across different menopausal stages, along with a higher prevalence of menopausal symptoms (20,28,110). These symptoms were associated with lower health-related quality of life (HRQoL) in both WLHIV and HIV-negative women (63). However, some studies reported no significant association between HIV status and menopausal symptoms (39), while other studies have reported an association (20). In South Africa, WLHIV and HIV-negative women did not show significant differences in the prevalence of menopausal symptoms, suggesting that menopausal symptoms in this study were not influenced by HIV status (63). However, the small sample size of HIV-positive women in these studies may have reduced the statistical power, limiting the ability to detect significant differences. Both HIV and menopause are associated with fatigue, depression, and cognitive changes, which might make clinical characterisation more difficult and delay diagnosis or treatment. The importance of integrated, comprehensive healthcare methods is made apparent by this overlap.

5. Limitations:

Our scoping review has several limitations. We found a limited number of studies on menopause experiences among women living with HIV (WLHIV) in Sub-Saharan Africa. Only a few studies met our inclusion criteria, which restricted the comprehensiveness of our review and our understanding of the challenges faced by WLHIV in this region. The initial pilot search was conducted in September 2023. However, due to time constraints, the literature search was not updated beyond October 2023, which is acknowledged as a limitation. Although the search was iterative, more recent studies may not have been included, which may influence the completeness of findings. Additionally, one reviewer (the author) carried out the screening and study selection, which may have introduced selection bias. To minimise this, the process was guided by a predefined protocol, and uncertainties were discussed with the supervisor. Nevertheless, dual independent screening would have further strengthened methodological rigour. Most of the included studies were from South Africa, Nigeria, and Zimbabwe, which limits the generalizability of our findings across the region. Many studies on HIV and menopause were not included in our review due to involving the wrong population and demographic. Future reviews could benefit from stratifying findings between LMIC and HIC settings for more comprehensive comparisons. Furthermore, the quality of studies may vary, with some studies exhibiting methodological limitations such as small sample sizes and potential biases, along with the absence of culturally adapted measurement tools in Sub-Saharan Africa, impacting the overall reliability and validity of our results. The majority of the evidence came from cross-sectional studies as compared to longitudinal studies. The lack of longitudinal studies restricts our understanding of menopause-related outcomes over time, making it difficult to establish causality or temporal relationships. Therefore, the exclusion of qualitative and mixed-methods studies may have reduced the comprehensiveness of the review, as qualitative approaches are particularly valuable for capturing the lived experiences and contextual influences on menopause among WLHIV. WLHIV who had undergone hysterectomy were also excluded, who may experience distinct menopausal trajectories. Our review also lacked a quality assessment, while not mandatory in scoping reviews, this limited our ability to comment on the strength of evidence. Future studies may consider a systematic review to avoid the risk of bias (61). Language bias is another concern, as our focus on English-language publications may have excluded relevant studies from Francophone or Lusophone African countries. Methodological heterogeneity across included studies also presented a challenge. Menopause definitions varied, with many relying solely on self-reporting. Future research should adopt internationally recognised criteria such as the STRAW+10 staging method, with biochemical confirmation of menopausal status. These inconsistencies limit comparability across studies and reduce the certainty of conclusions. However, despite these limitations, our scoping review included current literature on menopause-related issues among WLHIV in Sub-Saharan Africa without time restrictions, ensuring the findings are relevant to current circumstances.

6. Future recommendations:

The findings from our scoping review highlight areas for healthcare providers to improve care for WLHIV during menopause in Sub-Saharan Africa. Understanding the relationship between HIV and menopause requires further research on factors impacting WLHIV during their menopausal transition in Sub-Saharan Africa. However, studies are limited in this research area. Future longitudinal cohort studies are required to investigate temporal relationships. HIV-negative comparator groups from a broader range of countries within the Sub-Saharan region are essential to capture the diversity of menopausal experiences and health system contexts. Additionally, existing menopause symptom scales lack validation for Sub-Saharan African populations, necessitating the creation of culturally relevant instruments. Few studies address the lived experiences of WLHIV during menopause, suggesting the need for qualitative or mixed-methods research to understand how social and psychological factors also influence how WLHIV experience menopause. Future research should consider the impact of ART, comorbidities, sociodemographic factors such as smoking, obesity, education, race, and healthcare access on menopausal experiences and outcomes, emphasising the need for integrated care that aligns HIV and menopause services for ageing WLHIV.

7. Conclusions:

This scoping review provides an overview of the current state of knowledge on the menopausal experiences among women living with HIV (WLHIV) in Sub-Saharan Africa (SSA). Our findings highlight the significant impact of HIV on menopause and the unique challenges faced by WLHIV during menopause in this region. Studies found a high prevalence of early menopause, more severe vasomotor, somatic, and psychological menopause symptoms, and reduced BMD among WLHIV in SSA, increasing the risk of osteoporotic fractures. Limited evidence also suggests that obesity may increase symptom severity, though findings remain inconsistent.

Few studies capture the lived experiences of WLHIV during menopause, while broader contextual factors such as socioeconomic status and healthcare access may influence menopausal experiences, our review did not provide strong empirical evidence on this association in SSA populations. A key gap in Sub-Saharan Africa is the lack of longitudinal and qualitative studies, which limits understanding of causal pathways and lived experiences related to menopause. Another key gap is the lack of validated, culturally adapted measurement tools to assess menopausal symptoms for WLHIV in SSA, limiting the accuracy of symptom assessment. These gaps restrict a nuanced understanding of how WLHIV experience and manage menopause in diverse African contexts.

Our findings highlight the importance of considering HIV in managing menopause-related health issues to improve health outcomes and overall well-being. Future research is needed to explore how menopause care can be integrated into HIV services to address the specific needs of ageing WLHIV.

Overall, this review underscores that menopause is a critical but underexplored component of care for older WLHIV in Sub-Saharan Africa. The review highlights important implications for healthcare services in SSA, guiding healthcare providers in identifying new strategies to better support the unique needs of menopausal WLHIV in LMICs. Addressing the association between HIV and menopause in WLHIV through methodologically robust, contextually relevant research is critical to developing tailored health interventions and policies that improve the quality of life and health outcomes for an ageing population of WLHIV.

8. Declarations

8.1 Ethics declaration

Ethics approval was not necessary, considering that this dissertation synthesises the results of previously published research. No direct human participants were involved, or interventions, but the review of existing literature. The review ensured compliance with research standards.

8.2 Acknowledgements

I am grateful to the Lord for blessing me with the opportunity to pursue an education. Thank you to the Holy Spirit for ordering my steps and guiding me towards the finish line.

"I am confident of this, that He who began a good work in you will carry it on to completion until the day of Christ Jesus."- Philippians 1:6

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8.3 Conflicts of interest

The authors declare no conflicts of interest regarding the publication of this manuscript. All authors have no financial or personal relationships that could influence or bias the content of this work.

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8.5 Authors' contributions

Nokwanda Themba is the primary author of the scoping review and was responsible for the conception and design of the study, conducting the literature search, screening, and selecting the articles for inclusion, data extraction, analysis, and interpretation of the findings, and drafting and revising the manuscript. The final manuscript was conducted independently by the primary author.

8.6 Authors' information

Not applicable.

9. List of abbreviations

ANM	Age at natural menopause
ART	Antiretroviral therapy
BMD	Bone mineral density
BMI	Body mass index
cART	Combination antiretroviral therapy
DXA	Dual energy X-ray absorptiometry
EM	Early menopause
FMP	Final menstrual period
GPAQ	Global Physical Activity Questionnaire
HAART	Highly active antiretroviral treatment
HIC	High-Income Countries
HIV	Human immunodeficiency virus
HRQoL	Health-related quality of life
HRT	Hormone Replacement Therapy
JI	Joanna Briggs Institute
LMIC	Lower-Middle-Income Countries
MesH	Medical Subject Headings
MHT	Menopausal hormone therapy
MRS	Menopause Rating Scale
MT	Menopausal Transition
NCDs	Non-communicable diseases
PCC	Population, Concept, Context
POF	Premature ovarian failure
PRISMA	Preferred Reporting Items for Systematic reviews and Meta-Analyses
PLWH	People living with HIV
QoL	Quality of life
SSA	Sub-Saharan Africa
SWAN	Study of Women's Health Across the Nation
SWART	Stages of Reproductive Aging Workshop
SWEET	Study of Women Entering and in Endocrine Transition
UMIC	Upper-Middle-Income countries
VMS	Vasomotor symptoms
WHO	World Health Organization
WHOQOL-BREF	World Health Organization's Quality of Life instrument brief version
WWH	Women with HIV
WLHIV	Women living with HIV
WLWOH	Women living without HIV

10. References:

1. The World Health Organization (WHO). The World Health Organization (WHO). 2024 [cited 2024 Aug 17]. Global situation and trends. Available from: <https://www.who.int/data/gho/data/themes/hiv-aids>
2. UNAIDS. UNAIDS. 2024 [cited 2024 Aug 17]. Global HIV & AIDS statistics — Fact sheet. Available from: <https://www.unaids.org/en/resources/fact-sheet>
3. The World Health Organization (WHO). The World Health Organization (WHO). 2023 [cited 2024 Aug 17]. HIV statistics, globally and by WHO region. Available from: <https://cdn.who.int/media/docs/default-source/hq-hiv-hepatitis-and-stis-library/j0294-who-hiv-epi-factsheet-v7.pdf>
4. Mahy M, Autenrieth CS, Stanecki K, Wynd S. Increasing trends in HIV prevalence among people aged 50 years and older. *AIDS*. 2014 Nov;28(Supplement 4):S453–9.
5. Tariq S, Delpech V, Anderson J. The impact of the menopause transition on the health and wellbeing of women living with HIV: A narrative review. Vol. 88, *Maturitas*. Elsevier Ireland Ltd; 2016. p. 76–83.
6. Raffe S, Sabin C, Gilleece Y, Women Against Viruses in Europe (WAVE) EACS. Comorbidities in women living with HIV: A systematic review. *HIV Med*. 2022 Apr;23(4):331–61.
7. Marcus JL, Leyden WA, Alexeeff SE, Anderson AN, Hechter RC, Hu H, et al. Comparison of Overall and Comorbidity-Free Life Expectancy Between Insured Adults With and Without HIV Infection, 2000–2016. *JAMA Netw Open*. 2020 Jun 1;3(6):e207954.
8. Compston J. HIV infection and osteoporosis. *Bonekey Rep*. 2015 Feb 11;4.
9. Andany N, Kennedy VL, Aden M, Loutfy M. Perspectives on menopause and women with HIV. Vol. 8, *International Journal of Women's Health*. Dove Medical Press Ltd; 2016. p. 1–22.
10. Yisma E, Eshetu N, Ly S, Dessalegn B. Prevalence and severity of menopause symptoms among perimenopausal and postmenopausal women aged 30–49 years in Gulele sub-city of Addis Ababa, Ethiopia. *BMC Womens Health*. 2017 Dec 8;17(1):124.
11. Okhai H, Sabin C, Haag K, Sherr L, Dhairyawan R, Shephard J, et al. The Prevalence and Patterns of Menopausal Symptoms in Women Living with HIV. *AIDS Behav*. 2022 Nov 1;26(11):3679–87.
12. Andany N, Kennedy VL, Aden M, Loutfy M. Perspectives on menopause and women with HIV. *Int J Womens Health*. 2016;8:1–22.
13. Goedert JJ, Schairer C, McNeel TS, Hessol NA, Rabkin CS, Engels EA, et al. Risk of breast, ovary, and uterine corpus cancers among 85,268 women with AIDS. *Br J Cancer*. 2006 Sep 4;95(5):642–8.
14. Adam GP, Di M, Cu-Uvin S, Halladay C, Smith BT, Iyer S, et al. Strategies for improving the lives of US women aged 40 and above living with HIV/AIDS: an evidence map. *Syst Rev*. 2018 Feb 2;7(1):25.
15. Tariq S, Anderson J, Burns F, Delpech V, Gilson R, Sabin C. The menopause transition in women living with HIV: current evidence and future avenues of research. *J Virus Erad*. 2016 Apr 1;2(2):114–6.
16. Kojic EM, Wang CC, Cu-Uvin S. HIV and menopause: A review. Vol. 16, *Journal of Women's Health*. 2007. p. 1402–11.
17. Andany N, Kennedy VL, Aden M, Loutfy M. Perspectives on menopause and women with HIV. *Int J Womens Health*. 2016;8:1–22.
18. Woods NF, Mitchell ES. Symptoms during the perimenopause: prevalence, severity, trajectory, and significance in women's lives. *Am J Med*. 2005 Dec 19;118 Suppl 12B:14–24.

19. Boonyanurak P, Bunupuradah T, Wilawan K, Lueanyod A, Thongpaeng P, Chatvong D, et al. Age at menopause and menopause-related symptoms in human immunodeficiency virus–infected Thai women. *Menopause*. 2012 Jul;19(7):820–4.
20. Ferreira CE, Pinto-Neto AM, Conde DM, Costa-Paiva L, Morais SS, Magalhães J. Menopause symptoms in women infected with HIV: Prevalence and associated factors. *Gynecological Endocrinology*. 2007 Jan 7;23(4):198–205.
21. Looby SE, Shifren J, Corless I, Rope A, Pedersen MC, Joffe H, et al. Increased hot flash severity and related interference in perimenopausal human immunodeficiency virus-infected women. *Menopause*. 2014 Apr;21(4):403–9.
22. Friderichs T, Hall D. Postmenopausal symptoms in a group of rural Xhosa women. *South African Family Practice*. 2005 Jun 15;47(5):56–8.
23. Nkwo P, Onah H. Positive attitude to menopause and improved quality of life among Igbo women in Nigeria. *International Journal of Gynecology & Obstetrics*. 2008 Oct 18;103(1):71–2.
24. Kwawukume EY, Ghosh TS, Wilson JB. Menopausal age of Ghanaian women. *International Journal of Gynecology & Obstetrics*. 1993 Feb;40(2):151–5.
25. Yisma E, Eshetu N, Ly S, Dessalegn B. Prevalence and severity of menopause symptoms among perimenopausal and postmenopausal women aged 30–49 years in Gulele sub-city of Addis Ababa, Ethiopia. *BMC Womens Health*. 2017 Dec 8;17(1):124.
26. Ahmed MH, Bondje S, Jiwan R, Rawther F, Duku A, Husain NE, et al. Early menopause in acquired immunodeficiency syndrome. *J Res Med Sci*. 2021;26:122.
27. Suarez-García I, Alejos B, Pérez-Elías MJ, Iribarren JA, Hernando A, Ramírez M, et al. How do women living with HIV experience menopause? Menopausal symptoms, anxiety and depression according to reproductive age in a multicenter cohort. *BMC Womens Health*. 2021 Dec 28;21(1):223.
28. Madanhire T, Hawley S, Dauya E, Bandason T, Rukuni R, Ferrand RA, et al. Menopausal symptoms by HIV status and association with health-related quality of life among women in Zimbabwe: a cross-sectional study. *BMC Womens Health*. 2023 Jun 29;23(1):343.
29. Looby SE, Psaros C, Raggio G, Rivard C, Smeaton L, Shifren J, et al. Association between HIV status and psychological symptoms in perimenopausal women. *Menopause*. 2018 Jun;25(6):648–56.
30. Garbose RA, Wu J, Christianson MS, Robinson T, Gaines T, Shen W. Menopause symptoms delineated by HIV clinical characteristics in African American women with HIV. *Menopause*. 2020 Oct 19;28(2):189–97.
31. Tariq S, Delpech V, Anderson J. The impact of the menopause transition on the health and wellbeing of women living with HIV: A narrative review. Vol. 88, *Maturitas*. Elsevier Ireland Ltd; 2016. p. 76–83.
32. Looby SE, Shifren J, Corless I, Rope A, Pedersen MC, Joffe H, et al. Increased hot flash severity and related interference in perimenopausal human immunodeficiency virus-infected women. In: *Menopause*. Lippincott Williams and Wilkins; 2014. p. 403–9.
33. Schoenaker DAJM, Jackson CA, Rowlands J V, Mishra GD. Socioeconomic position, lifestyle factors and age at natural menopause: a systematic review and meta-analyses of studies across six continents. *Int J Epidemiol*. 2014 Oct;43(5):1542–62.
34. Fantry LE, Zhan M, Taylor GH, Sill AM, Flaws JA. Age of Menopause and Menopausal Symptoms in HIV-Infected Women. *AIDS Patient Care STDS*. 2005 Nov;19(11):703–11.
35. Hachfeld A, Atkinson A, Stute P, Calmy A, Tarr PE, Darling K, et al. Women with HIV transitioning through menopause: Insights from the Swiss HIV Cohort Study (SHCS). *HIV Med*. 2022 Apr 1;23(4):417–25.

36. de Pommerol M, Hessamfar M, Lawson-Ayayi S, Neau D, Geffard S, Farbos S, et al. Menopause and HIV infection: age at onset and associated factors, ANRS CO3 Aquitaine cohort. *Int J STD AIDS*. 2011 Feb 1;22(2):67–72.
37. Clark RA, Mulligan K, Stamenovic E, Chang B, Watts H, Andersen J, et al. Frequency of Anovulation and Early Menopause among Women Enrolled in Selected Adult AIDS Clinical Trials Group Studies [Internet]. Vol. 184, *The Journal of Infectious Diseases*. 2001. Available from: <https://academic.oup.com/jid/article/184/10/1325/833612>
38. Schoenbaum EE, Hartel D, Lo Y, Howard AA, Floris-Moore M, Arnsten JH, et al. HIV infection, drug use, and onset of natural menopause. *Clin Infect Dis*. 2005 Nov 15;41(10):1517–24.
39. Lui-Filho JF, Valadares ALR, Gomes DC, Amaral E, Pinto-Neto AM, Costa-Paiva L. Menopausal symptoms and associated factors in HIV-positive women. *Maturitas*. 2013;76(2):172–8.
40. Miller SA, Santoro N, Lo Y, Howard AA, Arnsten JH, Floris-Moore M, et al. Menopause symptoms in HIV-infected and drug-using women. Vol. 12, *Menopause*. 2005. p. 348–56.
41. Chan S, Gomes A, Singh RS. Is menopause still evolving? Evidence from a longitudinal study of multiethnic populations and its relevance to women's health. *BMC Womens Health*. 2020 Apr 19;20(1):74.
42. Calvet GA, Grinsztejn BGJ, Quintana M de SB, Derrico M, Jalil EM, Cytryn A, et al. Predictors of early menopause in HIV-infected women: a prospective cohort study. *Am J Obstet Gynecol*. 2015 Jun;212(6):765.e1-765.e13.
43. Imai K, Sutton MY, Mudo R, del Rio C. HIV and Menopause: A Systematic Review of the Effects of HIV Infection on Age at Menopause and the Effects of Menopause on Response to Antiretroviral Therapy. *Obstet Gynecol Int*. 2013;2013:1–11.
44. Tariq S, Anderson J, Burns F, Delpech V, Gilson R, Sabin C. The menopause transition in women living with HIV: current evidence and future avenues of research. *J Virus Erad*. 2016 Apr 1;2(2):114–6.
45. Kwawukume EY, Ghosh TS, Wilson JB. Menopausal age of Ghanaian women. *International Journal of Gynecology & Obstetrics*. 1993 Feb;40(2):151–5.
46. Okonofua FE, Lawal A, Bamgbose JK. Features of menopause and menopausal age in Nigerian women. *Int J Gynaecol Obstet*. 1990 Apr;31(4):341–5.
47. Anolue FC, Dike E, Adogu P, Ehirim C. Women's experience of menopause in rural communities in Orlu, Eastern Nigeria. *International Journal of Gynecology & Obstetrics*. 2012 Jul 28;118(1):31–3.
48. Nkwo P, Onah H. Positive attitude to menopause and improved quality of life among Igbo women in Nigeria. *International Journal of Gynecology & Obstetrics*. 2008 Oct 18;103(1):71–2.
49. Curno MJ, Rossi S, Hodges-Mameletzis I, Johnston R, Price MA, Heidari S. A Systematic Review of the Inclusion (or Exclusion) of Women in HIV Research. *JAIDS Journal of Acquired Immune Deficiency Syndromes*. 2016 Feb 1;71(2):181–8.
50. Loutfy MR, Sherr L, Sonnenberg-Schwan U, Walmsley SL, Johnson M, d'Arminio Monforte A. Caring for women living with HIV: gaps in the evidence. *J Int AIDS Soc*. 2013 Jan;16(1).
51. Ambikairajah A, Walsh E, Cherbuin N. A review of menopause nomenclature. *Reprod Health*. 2022 Jan 31;19(1):29.
52. Dominguez S, Branco T, Haruperi T. Considerations for the Long-Term Management of Women Living with HIV in Europe. *Antivir Ther*. 2013 Feb 1;18(2_suppl):45–52.
53. Chirwa M, Ma R, Guallar C, Tariq S. Managing menopause in women living with HIV: A survey of primary care practitioners. *Post Reprod Health*. 2017 Sep;23(3):111–5.

54. Tariq S, Anderson J, Burns F, Delpech V, Gilson R, Sabin C. The menopause transition in women living with HIV: current evidence and future avenues of research. *J Virus Erad.* 2016 Apr 1;2(2):114–6.
55. Munn Z, Peters MDJ, Stern C, Tufanaru C, McArthur A, Aromataris E. Systematic review or scoping review? Guidance for authors when choosing between a systematic or scoping review approach. *BMC Med Res Methodol.* 2018 Nov 19;18(1):143.
56. Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, et al. PRISMA Extension for Scoping Reviews (PRISMA-ScR): Checklist and Explanation. *Ann Intern Med.* 2018 Oct 2;169(7):467–73.
57. Peters MDJ, Marnie C, Tricco AC, Pollock D, Munn Z, Alexander L, et al. Updated methodological guidance for the conduct of scoping reviews. *JBIM Evid Synth.* 2020 Oct;18(10):2119–26.
58. Arksey H, O'Malley L. Scoping studies: towards a methodological framework. *Int J Soc Res Methodol.* 2005 Feb;8(1):19–32.
59. Mak S, Thomas A. Steps for Conducting a Scoping Review. *J Grad Med Educ.* 2022 Oct;14(5):565–7.
60. Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, et al. PRISMA Extension for Scoping Reviews (PRISMA-ScR): Checklist and Explanation. *Ann Intern Med.* 2018 Oct 2;169(7):467–73.
61. Pollock D, Peters MDJ, Khalil H, McInerney P, Alexander L, Tricco AC, et al. Recommendations for the extraction, analysis, and presentation of results in scoping reviews. *JBIM Evid Synth.* 2023 Mar;21(3):520–32.
62. Peters M, Godfrey C, McInerney P, Munn Z, Trico A, Khalil H. Chapter 11: Scoping reviews. In: *JBIM Manual for Evidence Synthesis.* JBIM; 2020.
63. Jaff NG, Snyman T, Norris SA, Crowther NJ. Staging reproductive aging using Stages of Reproductive Aging Workshop + 10 in black urban African women in the Study of Women Entering and in Endocrine Transition. *Menopause.* 2014 Nov;21(11):1225–33.
64. WHO. <https://www.who.int/news-room/fact-sheets/detail/menopause>. 2022. Menopause.
65. Agaba P, Meloni S, Sule H, Ocheke A, Agaba E, Idoko J, et al. Factors associated with early menopause among women in Nigeria. 2017.
66. Ó Breasail M, Gregson CL, Norris SA, Madanhire T, Jaff N, Crowther NJ, et al. Menopause is associated with bone loss, particularly at the distal radius, in black South African women: Findings from the Study of Women Entering and in Endocrine Transition (SWEET). *Bone.* 2022 Nov;164:116543.
67. Agaba PA, Meloni ST, Sule HM, Ocheke AN, Agaba EI, Idoko JA, et al. Prevalence and predictors of severe menopause symptoms among HIV-positive and -negative Nigerian women. *Int J STD AIDS.* 2017 Nov 14;28(13):1325–34.
68. Madanhire T, Goedecke JH, Ward KA, Jaff N, Crowther NJ, Norris S, et al. The Impact of Human Immunodeficiency Virus and Menopause on Bone Mineral Density: A Longitudinal Study of Urban-Dwelling South African Women. *Journal of Bone and Mineral Research.* 2023 May 1;38(5):619–30.
69. Madanhire T, Hawley S, Dauya E, Bandason T, Rukuni R, Ferrand RA, et al. Menopausal symptoms by HIV status and association with health-related quality of life among women in Zimbabwe: a cross-sectional study. *BMC Womens Health.* 2023 Jun 29;23(1):343.
70. Ellis C, Kruger HS, Viljoen M, Dave JA, Kruger MC. Factors associated with bone mineral density and bone resorption markers in postmenopausal hiv-infected women on antiretroviral therapy: A prospective cohort study. *Nutrients.* 2021 Jun 1;13(6).

71. Moslehi N, Shab-Bidar S, Mirmiran P, Hosseini F, Azizi F. Determinants of parathyroid hormone response to vitamin D supplementation: a systematic review and meta-analysis of randomised controlled trials. *British Journal of Nutrition*. 2015 Nov 14;114(9):1360–74.
72. Graham EE, Michala L, Hachfeld A, Moseholm E. Collection of menopause data in studies of women living with : A systematic literature review. *HIV Med*. 2024 Feb 30;25(2):174–87.
73. El Khoudary SR, Greendale G, Crawford SL, Avis NE, Brooks MM, Thurston RC, et al. The menopause transition and women's health at midlife: a progress report from the Study of Women's Health Across the Nation (SWAN). *Menopause*. 2019 Oct;26(10):1213–27.
74. Sourouni M, Zangger M, Honermann L, Foth D, Stute P. Assessment of the climacteric syndrome: a narrative review. *Arch Gynecol Obstet*. 2021 Oct;304(4):855–62.
75. Heinemann K, Ruebig A, Potthoff P, Schneider HPG, Strelow F, Heinemann LAJ, et al. The Menopause Rating Scale (MRS) scale: a methodological review. *Health Qual Life Outcomes*. 2004 Sep 2;2:45.
76. Stone L, Looby SE, Zanni M V. Cardiovascular disease risk among women living with HIV in North America and Europe. Vol. 12, *Current Opinion in HIV and AIDS*. Lippincott Williams and Wilkins; 2017. p. 585–93.
77. Sourouni M, Zangger M, Honermann L, Foth D, Stute P. Assessment of the climacteric syndrome: a narrative review. *Arch Gynecol Obstet*. 2021 Oct;304(4):855–62.
78. Heinemann K, Ruebig A, Potthoff P, Schneider HPG, Strelow F, Heinemann LAJ, et al. The Menopause Rating Scale (MRS) scale: a methodological review. *Health Qual Life Outcomes*. 2004 Sep 2;2:45.
79. Duff PK, Money DM, Ogilvie GS, Ranville F, Kestler M, Braschel MC, et al. Severe menopausal symptoms associated with reduced adherence to antiretroviral therapy among perimenopausal and menopausal women living with HIV in Metro Vancouver. *Menopause*. 2018 May;25(5):531–7.
80. Johnson TM, Cohen HW, Howard AA, Santoro N, Floris-Moore M, Arnsten JH, et al. Attribution of menopause symptoms in human immunodeficiency virus-infected or at-risk drug-using women. *Menopause*. 2008 May;15(3):551–7.
81. Andany N, Kaida A, de Pokomandy A, Yudin MH, Wang L, Kennedy VL, et al. Prevalence and correlates of early-onset menopause among women living with HIV in Canada. *Menopause*. 2020 Jan;27(1):66–75.
82. Chan S, Gomes A, Singh RS. Is menopause still evolving? Evidence from a longitudinal study of multiethnic populations and its relevance to women's health. *BMC Womens Health*. 2020 Dec 19;20(1):74.
83. Chirwa M, Taghinejadi N, Macaulay G, Mandalia S, Bellone C, Panay N, et al. Reflections on a specialist HIV menopause service: Experiences of managing menopause in women living with HIV. *HIV Med*. 2022 Apr 1;23(4):426–33.
84. Swann SA, King EM, Tognazzini S, Campbell AR, Levy SLA, Pick N, et al. Age at Natural Menopause in Women Living with HIV: A Cross-Sectional Study Comparing Self-Reported and Biochemical Data. *Viruses*. 2023 Apr 26;15(5):1058.
85. Gold EB, Bromberger J, Crawford S, Samuels S, Greendale GA, Harlow SD, et al. Factors Associated with Age at Natural Menopause in a Multiethnic Sample of Midlife Women [Internet]. Vol. 153, *American Journal of Epidemiology*. 2001. Available from: <https://academic.oup.com/aje/article/153/9/865/124589>
86. Bromberger JT, Matthews KA, Kuller LH, Wing RR, Meilahn EN, Plantinga P. Prospective Study of the Determinants of Age at Menopause. *Am J Epidemiol*. 1997 Jan 15;145(2):124–33.

87. Harlow BL, Signorello LB. Factors associated with early menopause. *Maturitas*. 2000 Apr 28;35(1):3–9.
88. Schoenbaum EE, Hartel D, Lo Y, Howard AA, Floris-Moore M, Arnsten JH, et al. HIV Infection, Drug Use, and Onset of Natural Menopause [Internet]. Available from: <https://academic.oup.com/cid/article/41/10/1517/347364>
89. Ferreira CE, Pinto-Neto AM, Conde DM, Costa-Paiva L, Morais SS, Magalhães J. Menopause symptoms in women infected with HIV: Prevalence and associated factors. *Gynecological Endocrinology*. 2007 Jan 7;23(4):198–205.
90. Okonofua FE, Lawal A, Bamgbose JK. Features of menopause and menopausal age in Nigerian women. *Int J Gynaecol Obstet*. 1990 Apr;31(4):341–5.
91. Schoenbaum EE, Hartel D, Lo Y, Howard AA, Floris-Moore M, Arnsten JH, et al. HIV infection, drug use, and onset of natural menopause. *Clin Infect Dis*. 2005 Nov 15;41(10):1517–24.
92. Ahmed M, Mital D, Abubaker NE, Panourgia M, Owles H, Papadaki I, et al. Bone Health in People Living with HIV/AIDS: An Update of Where We Are and Potential Future Strategies. *Microorganisms*. 2023 Mar 19;11(3):789.
93. Arnsten JH, Freeman R, Howard AA, Floris-Moore M, Santoro N, Schoenbaum EE. HIV Infection and Bone Mineral Density in Middle-Aged Women. *Clinical Infectious Diseases*. 2006 Apr 1;42(7):1014–20.
94. Matovu FK, Pettifor JM, Compston JE. HIV and Bone Health: Considerations for Menopausal Women Living with HIV in Sub-Saharan Africa. *Journal of Bone and Mineral Research*. 2020 Dec 1;38(5):617–8.
95. Gomes DC, Valadares ALR, de Moraes MJ, Lagrutta BB, Pinto-Neto AM, Costa-Paiva L. Low bone mass in human immunodeficiency virus-infected climacteric women receiving antiretroviral therapy: prevalence and associated factors. *Menopause*. 2015 Feb;22(2):224–30.
96. Cazanave C, Dupon M, Lavignolle-Aurillac V, Barthe N, Lawson-Ayayi S, Mehnen N, et al. Reduced bone mineral density in HIV-infected patients: prevalence and associated factors. *AIDS*. 2008 Jan 30;22(3):395–402.
97. Sharma A, Flom PL, Weedon J, Klein RS. Prospective study of bone mineral density changes in aging men with or at risk for HIV infection. *AIDS*. 2010 Sep 24;24(15):2337–45.
98. Yin MT, Shi Q, Hoover DR, Anastos K, Sharma A, Young M, et al. Fracture incidence in HIV-infected women: results from the Women's Interagency HIV Study. *AIDS*. 2010 Nov 13;24(17):2679–86.
99. Anastos K, Lu D, Shi O, Mulligan K, Tien PC, Freeman R, et al. The association of bone mineral density with HIV infection and antiretroviral treatment in women. *Antivir Ther*. 2007;12(7):1049–58.
100. Jacobson DL, Spiegelman D, Knox TK, Wilson IB. Evolution and predictors of change in total bone mineral density over time in HIV-infected men and women in the nutrition for healthy living study. *J Acquir Immune Defic Syndr*. 2008 Nov 1;49(3):298–308.
101. Pinto Neto LFS, Ragi-Eis S, Vieira NFR, Soprani M, Neves MB, Ribeiro-Rodrigues R, et al. Low bone mass prevalence, therapy type, and clinical risk factors in an HIV-infected Brazilian population. *J Clin Densitom*. 2011;14(4):434–9.
102. Yin M, Dobkin J, Brudney K, Becker C, Zadel JL, Manandhar M, et al. Bone mass and mineral metabolism in HIV+ postmenopausal women. *Osteoporosis International*. 2005 Nov;16(11):1345–52.
103. Carr A, Grund B, Neuhaus J, Schwartz A, Bernardino J, White D, et al. Prevalence of and risk factors for low bone mineral density in untreated <sc>HIV</sc> infection: a substudy of the <sc>INSIGHT</sc> Strategic Timing of AntiRetroviral Treatment (<sc>START</sc>) trial. *HIV Med*. 2015 Apr 25;16(S1):137–46.

104. Sharma A, Flom PL, Rosen CJ, Schoenbaum EE. Racial differences in bone loss and relation to menopause among HIV-infected and uninfected women. *Bone*. 2015 Aug;77:24–30.
105. Ashraf AN, Okhai H, Sabin CA, Sherr L, Haag K, Dhairyawan R, et al. Obesity in women living with HIV aged 45–60 in England: An analysis of the PRIME study. *HIV Med*. 2022 Apr 18;23(4):371–7.
106. Cao V, Clark A, Aggarwal B. Obesity and Severity of Menopausal Symptoms: a Contemporary Review. *Curr Diab Rep*. 2023 Dec 24;23(12):361–70.
107. Palacios S, Chedraui P, Sánchez-Borrego R, Coronado P, Nappi RE. Obesity and menopause. *Gynecological Endocrinology*. 2024 Dec 31;40(1).
108. Harlow SD, Gass M, Hall JE, Lobo R, Maki P, Rebar RW, et al. Executive summary of the Stages of Reproductive Aging Workshop + 10: addressing the unfinished agenda of staging reproductive aging. *Menopause*. 2012 Apr;19(4):387–95.
109. Soules MR, Sherman S, Parrott E, Rebar R, Santoro N, Utian W, et al. Stages of Reproductive Aging Workshop (STRAW). *J Womens Health Gend Based Med*. 2001 Nov;10(9):843–8.
110. Looby SE, Shifren J, Corless I, Rope A, Pedersen MC, Joffe H, et al. Increased hot flash severity and related interference in perimenopausal human immunodeficiency virus–infected women. *Menopause*. 2014 Apr;21(4):403–9.

Appendices

Appendix I: Research Protocol



Research Protocol

Title:	Menopause experiences among women living with HIV (WLHIV) in Sub-Saharan Africa: a scoping review
Author:	Nokwanda Themba
Supervisor:	Professor Landon Myer
Institution:	University of Cape Town



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1. List of abbreviations

AMH	Anti-Müllerian hormone
ANM	Age at natural menopause
ART	Antiretroviral therapy
BMD	Bone mineral density
BMI	Body mass index
cART	Combination antiretroviral therapy
DAX	Dual energy X-ray absorptiometry
EM	Early menopause
FMP	Final menstrual period
GPAQ	Global Physical Activity Questionnaire
HAART	Highly active antiretroviral treatment
HIV	Human immunodeficiency virus
HRQoL	Health-related quality of life
HRT	Hormone Replacement Therapy
JBI	Joanna Briggs Institute
MesH	Medical Subject Headings
MHT	Menopausal hormone therapy
MRS	Menopause Rating Scale
MT	Menopausal Transition
NCDs	Non-communicable diseases
PCC	Population, Concept, Context
POF	Premature ovarian failure
PRISMA	Preferred Reporting Items for Systematic reviews and Meta-Analyses
PLWHIV	People living with HIV
QoL	Quality of life
SSA	Sub-Saharan Africa
SWAN	Study of Women's Health Across the Nation
SWART	Stages of Reproductive Aging Workshop
SWEET	Study of Women Entering and in Endocrine Transition
VMS	Vasomotor symptoms
WHO	World Health Organization
WWH	Women with HIV
WLHIV	Women living with HIV
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2. Introduction

2.1 Background

Prevalence of HIV in Sub-Saharan Africa:

The World Health Organization (WHO) reported that by 2022, 39.0 million people worldwide were living with HIV, with 20.0 million women aged 15 and above (1). Sub-Saharan Africa remains disproportionately affected by the HIV epidemic, with 20.7 million people living with HIV (1,2). In 2021, South Africa had a population of 30,75 million, with 51.1% being female, and an overall HIV prevalence rate of 13.7%, resulting in 8.2 million people living with HIV (1).

Menopause and Women Living with HIV:

Menopause presents distinct challenges for women living with HIV (WLHIV), including physical and psychological effects, hormonal imbalances, and symptoms such as mood swings, urogenital issues, and vasomotor disturbance (3). These symptoms vary widely (4), and are shaped by biological, psychosocial, and cultural factors, resulting in unique experiences for each woman (5). WLHIV also tend to have lower estradiol levels, reduced ovarian reserves, and higher cardiovascular risks compared to HIV-negative women (6). Women living with HIV experience an accelerated onset and progression of age-related comorbidities, such as neurocognitive dysfunction, cardiovascular disease, and bone mineral disease, which can be worsened by HIV or its treatment (5). Research indicates that WLHIV may enter menopause earlier due to premature ovarian function loss, although findings on the age at menopause are inconsistent (7). Some studies show no significant difference in menopausal age between HIV-positive and HIV-negative women (8), while others suggest that menopause occurs earlier in women with HIV (9).

Epidemiological Context

In Sub-Saharan Africa, WLHIV face unique challenges during menopause, intensified by the complex relationship between menopause and HIV. Advancements in antiretroviral therapy have increased life expectancy for WLHIV (10), resulting in a growing population of older WLHIV reaching menopause age (11). The high burden of HIV complicates menopausal experiences for women due to factors such as limited healthcare access, rising poverty, poor socio-economic conditions, and cultural norms. Limited access to adequate nutrition and healthcare can worsen bone health, resulting in decreased bone mineral density and a higher risk of osteoporosis (12–14).



3. Literature review

3.1 Introduction

Menopause can cause a variety of physical and psychological symptoms, some of which may worsen for women with HIV. Women living with HIV (WLHIV) may experience menopause differently than women living without HIV. The complex relationship between menopause and HIV highlights the importance of understanding the unique challenges faced by WLHIV during menopause.

This literature review will explore current knowledge on both menopause and HIV, the effects of menopause on HIV disease progression, the impact of HIV on the experience of menopause in women, associated factors involved, comorbidities, disease management strategies, and the current experiences of menopause among WLHIV in the Sub-Saharan context.

Menopause

Menopause Definitions

Menopause marks the end of a woman's reproductive years (15), affecting her ovaries, hormones, and metabolism (16), and is often associated with various physical, emotional, and psychological changes (14). Menopause can occur naturally or be induced through medical interventions such as surgery, chemotherapy, or pelvic radiation therapy (17). Clinically, menopause is defined as 12 consecutive months of amenorrhea (18), determined retrospectively (19) from the final menstrual period (FMP). This phase involves the cessation of ovarian follicular function (15,20,21), depletion of ovarian follicles, and a decline in estradiol and progesterone production (10). The World Health Organization (WHO) defines natural menopause as the permanent cessation of menstruation due to the loss of ovarian follicular activity (15,22), confirmed after 12 months of amenorrhea not caused by induced menopause. Induced menopause occurs as a result of surgical procedures, such as the removal of both ovaries (hysterectomy or oophorectomy), or through iatrogenic ablation of ovarian function, which can happen due to treatments such as chemotherapy or radiation therapy (5,23). It may also arise from other pathological or physiological factors (9,24). It is essential to differentiate induced menopause from amenorrhea, which is characterized by the absence of menstruation for at least three months. This condition is frequently seen in women living with HIV and is often linked to anovulation or wasting (7).

The menopausal transition, the period before the FMP, is characterized by menstrual cycle variability (23). This transition is divided into early and late phases, marked by increasing follicle-stimulating hormone (FSH) levels and decreasing estrogen levels. The early postmenopausal stage encompasses the initial five years after menopause, while the late postmenopausal stage extends from five years after menopause until the end of life (17). FMP is preceded by the stage of



menopausal transition, divided into an early and late phase. In these phases, there is an increase in FSH levels and a decrease in estrogen levels. The early postmenopausal stage spans the initial five years after menopause, while the late postmenopausal stage extends from five years after menopause until the end of life (17).

Premature menopause (FMP < 40 years), the cessation of ovarian function occurring before the age of 40 (18) in women who exhibit symptoms such as amenorrhea, and infertility (25), is defined as menopause occurring at an age below two standard deviations from the mean established for the reference population (5). It is also recognized as premature ovarian failure (POF) or premature ovarian insufficiency (POI) (26,27), although POF may not be permanent (17).

Pre-menopause is defined as the entire reproductive period before the FMP (17), characterized by normal fertility function (15). The term is often used ambiguously to indicate the stage after menarche, one or two years immediately before menopause or the entire reproductive period preceding menopause (15,24).

Perimenopause, the first indication of menopause, is described as the period preceding and surrounding menopause (28), beginning with early menopause transition and ending 12 months after the FMP. This phase is marked by substantial hormonal changes, irregular menstrual patterns, and menopausal symptoms, often lasting for several years (15,20,24). Physiological changes signalling the start of perimenopause, such as decreasing estradiol levels, increasing FSH levels, and irregular menstrual cycles, typically begin in women's mid-40s (29). The term "climacteric," previously interchangeable with perimenopause, was reintroduced by The Council of Affiliated Menopause Societies (CAMS) in 1999 to encompass a broader phase extending before and after perimenopause, signifying the transition from reproductive to non-reproductive states (23,24).

Post-menopause is defined as the stage beginning 12 months after the final menstrual cycle (15) regardless of whether menopause was induced, spontaneous or artificial. The early postmenopausal stage encompasses the initial five years following menopause, whereas the late postmenopausal phase continues from five years after menopause until the end of life (17). [Table 1](#) provides an overview of the most common terminologies encountered in the scientific literature relating to menopause in our scoping review, followed by the STRAW + 10 staging system criteria used to define menopausal stages in [Figure 1](#).



Table 1: Key terms and definitions in the scoping review.

Terms	Definitions
Menopause	- a natural process characterized by the degeneration of ovarian follicles and the occurrence of FMP (28). - diagnosed retrospectively after a consecutive 12-month absence of menstruation after the FMP (15,17,20).
Menarche	the first menstrual cycle (30).
Natural Menopause	- characterized by the permanent cessation of menstruation after 12 consecutive months of amenorrhea (17). - diagnosed retrospectively with no other pathological or physiological causes resulting from a decline in ovarian follicular activity (24,28,31)
Early menopause	menopause occurring between the age of 40 and 45 (FMP 40–44 years) (26).
Early menarche	the onset of the first menstrual period at 11 years of age or younger (< 11 years) (32,33).
Surgical menopause	the surgical removal of both ovaries (bilateral oophorectomy) before the onset of natural menopause (26).
Induced menopause	menstruation cessation resulting from surgical removal of both ovaries (with or without hysterectomy) or the iatrogenic ablation of ovarian function (i.e. chemotherapy or radiation therapy) (5).
Menopausal transition	- occurs before the FMP involving high variability in menstrual cycle patterns (23). - begins with irregularities in cycle length and ends with the FMP. - characterized by changes in menstrual cycles and hormone levels (i.e. gradual FSH level increase) (34).
Post-menopause	- the stage that starts 12 months after the final menstrual cycle (15). - characterized as the period starting from 5 years after the FMP (34).
Perimenopause	- the transitional phase before FMP marked by the onset of menopausal symptoms, irregular menstrual cycles and hormonal fluctuations (15,26). "around the menopause" (34); the initial signs of menopause onset continuing until at least one year after FMP (17).
Premenopause	the entire reproductive period after menarche but before the FMP, before entering menopausal stages, characterized by normal fertility function (15,17).
Premature menopause	natural menopause before the age of 40 (FMP < 40 years) (17,18).
Premature ovarian failure (POF)	ovarian function cessation before the age of 40, characterized by amenorrhea, hypergonadotropic hypogonadism, and infertility (25).
Premature ovarian insufficiency (POI)	the onset of menopause before the age of 40 (26,27)

MENARCHE					MENOPAUSE (final menstrual period)				
STAGES	-5	-4	-3b	-3a	-2	-1	+1a+1b	+1c	+2
TERMINOLOGY	PREMENOPAUSE (REPRODUCTIVE)				MENOPAUSAL TRANSITION		POSTMENOPAUSE		
	EARLY	PEAK	LATE		EARLY	LATE	EARLY		LATE
					PERIMENOPAUSE				
PRINCIPAL CRITERIA	variable to regular*	regular*	regular*	subtle changes in flow or length	variable length ‡	60 or more days of amenorrhea			
SUPPORTIVE CRITERIA									
	Endocrine								
	FSH		low	variable*	variable*†	>25 IU/L†	variable†	stabilizes	
	AMH		low	low	low	low	low	very low	
	Inhibin B			low	low	low	low	very low	
Antral Follicle			low	low	low	low	very low	very low	
DESCRIPTIVE CHARACTERISTICS									
Vasomotor symptoms						likely	most likely		
Urogenital atrophy									symptoms increasing
STAGE DURATION	variable				variable	1-3 years	2 years	3-6 years	until demise
# regular menstruation, defined by the number of menstrual cycles per 3 months ‡ variable length persistent, seven or more day difference in length of consecutive cycles									

Figure 1 :The STRAW + 10 staging system (19,170).

Early menopause

Early Menopause is defined as the cessation of menstruation between the ages of 40 and 44 (26). The World Health Organization states that menopause typically occurs between ages 45 and 55 as a normal part of aging for most women. In developed countries, the average onset is between 50 and 52 years, although there is considerable geographic variation worldwide (5). In the Western world, the average age for menopause is 51.4 years, primarily influenced by genetic factors (17). Predictions for the age at natural menopause predominantly stem from studies conducted in Western populations and Caucasian women. However, findings from an international study across 11 countries found that the median age for natural menopause is 50 years, with a range of 49 to 52 years (36).

Studies on women living with HIV suggest that menopause may start earlier, often between the ages of 46 and 47, compared to women who are HIV-negative (18). The age of menarche, which is associated with body mass should not be confused with age at menopause (17). Early menarche has been associated with a higher risk of both early menopause and premature natural menopause (37,38). Various studies have highlighted that the age at natural menopause (ANM) varies among populations, showing differences across geographical regions and ethnic groups (39). A systematic



review and meta-analysis across six continents supported this finding, attributing the variations in ANM to geographical regions (32). Additionally, a longitudinal study involving multiethnic populations found wide variability in menopausal age within each population, with no significant differences between populations (39).

The onset of menopause in women living with HIV may occur at a younger age compared to women without HIV, influenced by various factors. Socioeconomic status, lifestyle choices, and cultural norms are factors that impact the age of onset (40). Common lifestyle factors, such as smoking, stress, diet, substance abuse, genetics, race/ethnicity and low socioeconomic status have been suggested as potential predictors associated with early menopause (18,37,41,42). Additionally, age at natural menopause (ANM) is postponed among individuals with higher levels of education and particular professions (43). While some studies indicate an insignificant impact of these factors on the variability in the onset of natural menopause (18,42), others highlight the significant role of ethnicity in the age of menopause.

Women of African descent are at a greater risk of early menopause (18), with many African women experiencing menopause at an earlier age (37,44). Studies conducted in Ghana and South Africa indicate that African women typically reach menopause earlier than their Caucasian counterparts, with mean menopausal ages around 48 years (45,46). A study examining black South African women aged 40-60 revealed minor differences in menopausal age between black and white women, with rural women averaging 49.5 years and urban women 48.9 years (47). In contrast, a smaller study in Nigeria found the mean age of menopause to be 52.8 years (36,48).

A population-based cohort study found that African American women had a higher likelihood of entering the initial menopause transition phase compared to Caucasian women (49). Non-Caucasian women tend to experience menopause earlier than Caucasian women, with Japanese women undergoing natural menopause at a later age compared to women of other racial/ethnic backgrounds. Women of Hispanic, African American, and Mexican heritage tend to reach menopause 6–12 months earlier than Caucasian women, while women of Japanese and Malaysian descent report a median menopausal age similar to women of European descent (36). A retrospective analysis of the Swiss HIV Cohort Study found that black women were four times more likely to have early menopause than those of other ethnicities, with 52.2% of black women experiencing early menopause compared to women from other ethnicities, despite factors such as HIV or smoking not impacting the age of menopause (27). Although specific differences in the timing of natural menopause among different racial and ethnic groups remain unclear (42), research suggests that African American women undergo natural menopause at an earlier age than white women (9) and non-Latina Whites, while Asian American women experience it later, partly due to psychological stress (9,42).



Psychosocial stress has been reported to be associated with earlier menopause. Stressful life events had no significant impact on menopausal age, although African American women who reported social stress had menopause earlier than other women (50). Women experiencing economic distress during both childhood and adulthood had a 1.75 times higher incidence of perimenopause and an earlier onset of menopause compared to women without economic distress (51). It has been suggested that menopause age is not associated with race, socioeconomic status, education, height, weight, age at menarche, or age at the last pregnancy (17). Although studies have found low socioeconomic class, marital status, unemployment, lower education levels, low body weight, infertility and having fewer children, have been inconsistently associated with earlier natural menopause (36). Early menopause has been associated with several factors, including sociodemographic, lifestyle, reproductive, and medical factors, which increase the risk of early natural menopause in HIV-positive individuals, although studies on early menopause (EM) in women living with HIV (WLHIV) particularly in Sub-Saharan Africa, are limited (14). Studies in the United States have observed that indicators such as lower socioeconomic status, lower education levels and higher unemployment rates, are associated with earlier menopause (9). However, no association between menopause onset and factors such as race/ethnicity, education level, employment status, age at menarche, BMI, alcohol consumption, cigarette smoking, stressful life events, or depressive symptoms was found (9).

A prospective cohort study found that factors such as ethnicity, HIV-related immunodeficiency, and IDU were associated with early menopause. However, ART usage, smoking, high viral load, lower CD4 count at nadir, transition to AIDS stage, and cohort enrolment duration were not found to be associated with menopause onset. Early menopause was more common in drug users and occurred at a younger age in women of African descent. Higher levels of immunosuppression have often been associated with earlier menopause, though factors like smoking, low education levels, and early menarche were not statistically significant (18).

Furthermore, there is evidence associating weight-loss programs with early menopause. An early start of menopause has been associated with weight loss diets (36). Dietary habits, such as being vegetarian, has been associated with earlier onset of menopause. Vegetarians experienced a mean age of 44.7 years compared to 47.9 years for non-vegetarians, though this pattern was not observed in South African black women (47). A prospective study found that African American ancestry, smoking, and following a weight-loss regimen were associated with earlier menopause, while moderate exercise or regular physical activity did not negatively affect menopausal age (50). Studies have shown that smoking increases the risk of early menopause (52). Smoking status and BMI influenced the age at natural menopause among black urban South African women, with current smoking being associated with earlier menopause and higher BMI with later menopause (53).



Cigarette smoking is a significant predictor of an earlier age at menopause onset, with smokers experiencing menopause 1-2 years earlier than nonsmokers (9,36). Heavy smokers experience menopause at an average age of 47.6 years, while non-smokers at 49.4 years (47). A prospective cohort study conducted in Brazil found that cigarette smoking and early menarche (<11 years) were significantly associated with earlier onset of natural menopause (54). However, factors such as race/ethnicity, education level, monthly family income, parity, oral contraceptive use, alcohol and cocaine consumption, BMI, type 2 diabetes, hypothyroidism, and cART use did not emerge as significant predictors of an earlier age at natural menopause in some studies (54).

Final Menstrual Period

The age at the final menstrual period (FMP) can differ based on race/ethnicity and various demographic and lifestyle factors, with smoking playing a significant role. Maternal age at menopause is also associated with the age at FMP, although limited longitudinal studies have explored this relationship (29). In white women from industrialized countries, the age at FMP typically ranges between 50 and 52 years, with some indications of a slight increase in recent cohorts (29). However, the mean age at FMP varies across different populations. A study in Zaria, Nigeria, reported a mean FMP age of 46.1 years, while recent research conducted in Europe estimated menopausal age at 54.0 years(53). In a larger Nigerian study ($n = 402$), the mean FMP age of 49.4 years(53), and in a smaller sample ($n = 152$), Ghanaian women had a mean FMP age of 48.05 years (45,53).

Anti-Müllerian hormone (AMH) is an important marker for menopausal transition and a reliable indicator of ovarian reserve and gonadal aging, particularly useful for predicting the age at the FMP in HIV-positive women (55). Higher AMH levels indicate the quantity of primordial follicles present in the ovaries while decreasing AMH levels with age signify a natural decline in ovarian function and reproductive capacity (55). AMH also affects the growth and selection of ovarian follicles during the menstrual cycle, regulating the cycle and follicular development. Healthcare professionals can use AMH levels to identify HIV-positive women at risk of menopausal onset and provide individualized treatment by adjusting therapies according to their expected age at FMP (55).

A longitudinal study conducted as part of the Study of Women's Health Across the Nation (SWAN) found no significant variations in both age at FMP and natural menopause based on race or ethnicity after accounting for socioeconomic status, lifestyle factors, and health indicators. However, higher educational levels were associated with a later onset of natural FMP, while lower educational levels were associated with an earlier age of menopause. Employment during the follow-up period correlated with a delayed age at FMP, and a higher baseline weight was also associated with a later age at FMP. These findings highlight the significant impact of health and socioeconomic factors such



as education level, oral contraceptive use, weight, and employment status on the timing of natural menopause (29).

In contrast, a study of Women Entering and in Endocrine Transition (SWEET) conducted among black urban South African women observed a negative correlation between the age at FMP and educational level, contradicting prior research associating younger menopausal age with lower education levels (53). There is limited research accurately determining the mean age at FMP and staging the menopausal transition (MT) in women from Sub-Saharan Africa (53).

Menopause Transition

Menopausal transition (MT) describes a complex physiological process characterized by decreased ovarian synthesis of estrogen and progesterone, reduced levels of testosterone, lifelong changes in bone mineral density, and symptoms including hot flashes and depression (3,56). Hormonal changes and increased inflammation, particularly due to estrogen depletion, contribute to bone health deterioration, which can lead to higher rates of bone loss (57). Reduced levels of reproductive hormones may worsen symptoms throughout MT, intensifying the transition and increasing symptom severity (58). Increased FSH, reduced inhibin B, estradiol levels, race and current smoking are predominant factors affecting the onset of the earliest transition stage, defined by cycle length changes lasting longer than seven days (49). Additionally, studies have shown that MT is associated with physiological changes that could increase the risk of cardiometabolic disorders (53).

The age of onset of MT is a significant predictor of the duration of each transition stage, with increasing age as a substantial indicator of progression through menopausal stages apart from the earliest menopausal stage (49,59). In the multi-racial/ethnic SWAN cohort, findings indicated that women who start MT at older ages tend to have shorter durations for each transition stage (59). However, whether an earlier onset of menopause is associated with an earlier entry into the transition phase has not been established (49).

A woman's advancement through MT is best assessed by monitoring menstrual cycle patterns (49), which forms the foundation for categorizing women in epidemiological research (10). A woman is classified as being in the "early" transition phase if she misses a menstrual period or experiences a cycle irregularity of more than seven days unless she has had three consecutive months of amenorrhea. Following three months, and up to eleven months of amenorrhea, the woman is classified as in the late transition phase and is considered postmenopausal after twelve months of complete menstrual cycle absence (10). The median age for late perimenopause onset is 47.5 years (29). Women who have encountered three months of amenorrhea have a high probability (approximately 95%) of transitioning to post-menopause within the subsequent four years (10).



Smoking is a significant predictor of early MT entry (49), associated with an earlier onset and shorter duration of MT, impacting both its timing and duration. A higher BMI is associated with a delayed onset of MT but not its duration. Previous research has shown that smokers tend to reach their final menstrual period at a younger age (59). In the Penn Ovarian Aging, current smoking increased the risk of transitioning through each stage of MT by approximately 30% (49). Smokers showed a younger age of onset and a shorter early MT, leading to an overall reduced MT duration. Specifically, current smokers had a lower median age of MT onset (46.05 years) compared to non-smokers (47.27 years) and exhibited shorter durations for both the early MT and the total MT. These findings highlight the adverse effects of smoking on ovarian function, indicating an accelerated process of ovarian aging due to smoking (59). Quitting smoking could benefit HIV-infected women approaching menopause, as smoking is associated with an earlier age at the final menstrual period (55).

African American women had longer MT durations compared to white women, although not statistically significant, with previous studies showing inconsistent associations between race/ethnicity and age at menopause (59). Although no apparent racial differences in progression to later phases were observed in this study, race significantly impacted the onset of the first transition stage (49). Additionally, women with lower education levels experienced shorter early MT durations than those with higher education levels, suggesting that lower socioeconomic status may negatively impact menstrual function (59).

Menopause Symptoms

Symptoms commonly associated with both menopause and HIV include hot flashes, night sweats, fatigue, sleep disturbances, mood changes, and vaginal dryness (60). Distinguishing between menopausal symptoms from those of HIV can be difficult due to symptom overlap, which may be influenced by various factors (60). It is also challenging to differentiate between perimenopausal symptoms and those attributed to HIV or antiretroviral treatment (ART) (61–63).

However, there are some general differences that can help distinguish between menopause and HIV-related symptoms. Menopause symptoms often include hot flashes, vaginal dryness, sleep disturbances, and alterations in psychological and cognitive functioning (60). In contrast, symptoms associated with HIV may involve peripheral neuropathy, which presents as numbness, tingling, or pain in the hands or feet, along with fatigue, headaches, fever, sore throat, and diarrhea (64). These symptoms can vary from person to person and across different cultures, influenced by factors such as aging, hormonal changes, and societal norms (15).

In high-income countries, common symptoms include vasomotor symptoms such as hot flashes, vaginal dryness, insomnia, fatigue, and joint pain (15). A possible protective factor against severe symptoms is the association between older age at menarche and less moderate and severe menopausal symptoms (65). Studies on Nigerian women have reported symptoms such as joint and



bone pain, hot flushes, insomnia, anxiety, urinary issues, fatigue, and dyspareunia. Similarly, menopausal Ghanaian women commonly report fatigue, sleep disturbances, palpitations, weight gain, hot flushes, and irritability (15).

Approximately 85% of perimenopausal women without HIV report experiencing menopausal symptoms (66) that impact their quality of life (67,68). Psychological symptoms, particularly depression and anxiety are highly prevalent in perimenopausal women living with HIV (69–71). Mood swings, insomnia, dry vagina, hot flushes, and night sweats are common during the perimenopausal stage (19). Other physical symptoms during menopause include headaches, fatigue, joint and bone pain, breast tenderness, irregular vaginal bleeding, and menorrhagia. Psychological symptoms including fatigue, irritability, depression, memory loss, and poor focus are also common. These symptom experiences may be substantially altered or aggravated in women who are HIV-positive (19).

The frequency and severity of vasomotor symptoms are impacted by multiple factors, including ethnicity. African American women typically experience hot flushes more frequently than White American women, whereas Japanese women generally report fewer symptoms overall (72). Studies from various locations, such as Iran and Korea, have found variations in menopausal symptoms across different ethnic, cultural, and socioeconomic backgrounds, suggesting the importance of multiple factors on menopausal experiences (65,73,74). Research from Europe, North and South America, and the United States supports the association between worse health-related quality of life (HRQoL) and somatic, psychological, and menopausal symptoms (65,75–77).

Menopausal symptoms in WLHIV in Nigeria are similar to those observed in other populations and previous studies conducted in Europe (58,78–80). However, the severity of symptoms such as hot flashes, cardiac issues, and bladder problems did not differ based on HIV status (58). Various factors contribute to the variability in menopausal symptoms, including fluctuations in estrogen levels, individual attitudes toward menopause, sociocultural and economic influences, and increased physical and psychological stress (58). Symptoms like mood swings, depression, and anxiety can significantly affect women's psychological well-being, and socio-cultural factors may influence how mental health is addressed during menopause (13).

Severe menopausal symptoms are significantly associated with lower quality of life, decreased mental health, and less engagement in HIV treatment (65). However, research is contradictory. A cross-sectional study in England involving women with HIV aged 45-60 found no differences in health-related quality of life between women with HIV and pre-menopausal women in the general population. However, perimenopausal women and those experiencing more severe menopausal symptoms had lower HRQoL. Furthermore, a high prevalence of pain was reported, with factors such



as peri-menopausal status, current smoking, number of comorbid conditions, and longer HIV duration independently associated with increased pain reports (20).

In Zimbabwe, a study observed that menopausal symptoms are prevalent among urban-dwelling women during the menopausal transition, with HIV-positive women exhibiting a higher prevalence of moderate to severe symptoms compared to those without HIV, particularly in terms of physical and psychological symptoms. Common menopausal symptoms include joint and muscle pain, irregular body temperature, physical and mental fatigue, and sexual difficulties. Symptoms such as joint/muscle soreness, sleep disturbances, heart discomfort, body temperature irregularities, irritability, anxiety, and mood disorders were notably associated with poorer HRQoL. Menopausal symptoms negatively impacted HRQoL, with the most severe symptoms being associated with HIV infection and factors such as alcohol consumption, unemployment, and food insecurity (65).

Women transitioning from premenopausal to later menopausal phases may encounter reduced cognitive function in areas such as learning, memory, and attention/working memory. Cognitive function is significantly impacted by menopausal stage in women, including WLHIV, many of whom experience cognitive deficits that were clinically significant, especially during the premenopausal and postmenopausal stages (81).

A study in Addis Ababa, Ethiopia, focusing on perimenopausal and postmenopausal women aged 30-49, found that the most commonly reported menopausal symptoms were somatic (65.9%), followed by psychological (46.0%) and urogenital (30.5%). Hot flushes, difficulty falling asleep, depressive mood, irritability, and anxiety were predominant symptoms. Postmenopausal women exhibited higher scores in somatic, psychological, and urogenital subscales compared to perimenopausal women (15). Hot flushes were reported by a substantial number of rural Xhosa women (80%), of whom 20% reported their symptoms were severe, and 69% reported experienced night sweats. Compared to studies conducted in other regions, rural Xhosa women had a higher prevalence of vasomotor symptoms than in urban African women (13).

Increased irritability has been associated with late menopause among urban-dwelling South African black women, consistent with previous research on the prevalence and severity of menopausal symptoms. The study found that women in the late reproductive stage had greater prevalence and more severe cases of vasomotor symptoms (VMS), potentially influenced by cultural differences in reporting hot flushes. Menopausal stage was strongly correlated with VMS, with premenopausal women showing greater irritability and postmenopausal women experiencing depressive episodes. Perimenopause has been associated with an increased risk of depression and mood disorders (53).

Weight gain and increased body fat are prevalent outcomes of the hormonal and metabolic changes that occur during the transition from perimenopause to post menopause. Consequently, a growing number of middle-aged women are becoming obese due to these factors. A cross-sectional study of



middle-aged Korean women revealed that obese women were significantly more likely to experience moderate to severe physical symptoms compared to those of normal weight or overweight (82). Additionally, obese women exhibited a greater susceptibility to moderate-to-severe vasomotor symptoms during the postmenopausal phase. Moreover, obese women reported a higher frequency of menopausal symptoms, with the specific symptoms varying by menopausal stage. In postmenopausal women, obesity was significantly linked to vasomotor symptoms such as sweating and hot flashes, while in perimenopausal women, it was associated with physical symptoms like weight gain and bloating (82).

Obesity was found to be an important risk factor for vasomotor symptoms (VMS) among black urban South African women going through the menopausal transition, notably in the late menopausal transition and early post menopause stages. Elevated FSH levels were also found to be correlated with VMS (53). Furthermore, an association between underweight and a later menopause was found (27). Increased levels of physical activity were shown to be negatively associated with the onset of menopause, suggesting that increased levels of physical activity may postpone menopause and its onset (9).

A study of Swedish middle-aged women aged 50-64 years, including both premenopausal and postmenopausal participants, found that higher education levels were associated with a greater risk of being symptom-free. Conversely, factors such as unemployment, physical inactivity, being unmarried, higher body weight, cardiovascular diseases, and a history of cancer were independently associated with an increased risk of somatic symptoms (83).

HIV and obesity together may increase the risk of developing comorbidities such as diabetes, cardiovascular disease, and fatty liver disease, specifically for postmenopausal women (84). However, a previous study observed that postmenopausal women with HIV had a lower BMI than non-HIV women (85). Weight gain additionally has a significant impact on HIV-positive individuals' health outcomes, associating with conditions including liver problems, kidney disease, and cardiovascular disease (86–88). Studies conducted in the UK has shown a relationship between obesity and black African ethnicity among individuals with HIV, while findings from the Women's Interagency HIV Study (WIHS) indicate that African American women in the US have higher BMIs compared to white women (88–90). However, the factors contributing to obesity among women of black African and other black ethnicities with HIV remain uncertain (84).

Bone health

Bone mineral density (BMD) is a crucial element of overall health. Low BMD can lead to conditions like osteoporosis, which increases the risk of fractures. Menopause serves as a significant marker for bone loss and low BMD in postmenopausal women living with HIV (25). The onset of menopause results in decreased estrogen levels, a hormone critical for maintaining and safeguarding bone



health (92) This decline leads to increased bone loss, osteoporosis, and a higher risk of fractures (93). Estrogen deficiency is a key factor in age-related bone loss in both men and women, as well as in postmenopausal women. It is recognized as the primary contributor to the reduction in cortical bone density and is vital for regulating bone metabolism and inhibiting bone turnover (94).

The reduction in estrogen levels among HIV-positive women can have a major effect on bone health (95). The absence of estrogen's advantageous impact on dyslipidaemia, cardiovascular disease (CVD), and bone density loss could place HIV-positive peri- and postmenopausal women at higher risk (96). Additionally, due to the combined effects of estrogen loss and HIV, postmenopausal women are at higher risk for developing osteoporosis. Menopause-related estrogen depletion commonly results in decreased bone mineral density (BMD) and increase the risk of osteoporosis. The decrease in estrogen levels can exacerbate bone-related problems in HIV, which is already associated with a higher risk of osteopenia and osteoporosis (95).

Osteoporosis is characterized by weak and brittle bones that are susceptible to fractures, is more likely to develop due to the rapid decline in BMD during and after menopause (97), particularly affecting postmenopausal women (98). Understanding the effects of menopause on bone mineral density is important to develop effective prevention and treatment strategies (99), as the need for maintaining bone health increases after menopause (100). Additionally, the prevalence of bone disorders among individuals living with HIV in Sub-Saharan Africa, the region with the highest rates of HIV infection, is not well understood, highlighting the need for further research to address the bone health needs of this population (101).

Multiple studies have demonstrated that WLHIV exhibit low BMD (68,69) and face a higher risk of osteoporosis and fractures compared to women without HIV (70,71). HIV infection is associated with an increased risk of developing osteopenia and osteoporosis (29,34,72–74). In resource-rich environments, individuals with HIV experience fracture rates ranging from 30% to 70% (75–79), along with abnormalities in bone formation and mineralization that affect trabecular regions in cortical areas (115). The low BMD observed in HIV-infected individuals is influenced by various osteoporosis risk factors, antiretroviral therapy, and HIV-related factors (34,81–83).

A cross-sectional study conducted in Nigeria found that osteoporosis was more prevalent in women over the age of 40 years (91). Additionally, a meta-analysis indicated that the prevalence of osteoporosis among individuals with HIV infection was 15% (34). According to research, individuals living with HIV have a 15% prevalence of osteoporosis (33,34), which may develop earlier (25,35). The prevalence of fracture risk in HIV-positive patients is significantly higher than that of those without HIV (90). The majority of research on bone disease in WLHIV primarily comes from North America (70). While research on fractures in Africa is limited, studies from well-resourced settings consistently indicate that HIV infection is associated with low BMD and increased risk of



fractures (92–94). The 2010 clinical guideline from the National Osteoporosis Foundation of South Africa (NOFSA) indicates that the prevalence of osteoporosis among white, Asian, and mixed-race groups in South Africa is similar to that found in developed countries, whereas it is less prevalent in black populations (40). A study conducted in rural South Africa revealed that osteoporosis is common among individuals over the age of 50, showing a significant association between HIV and osteoporosis. Among women with HIV, 37% were found to have osteoporosis of the femoral neck. Independent factors associated with lower BMD included older age, female gender, and HIV infection (95). A prospective study on Gambian adults found a significant decline in volumetric BMD and bone strength index (BSIc) at the radius, with women over 50 experiencing a 4% annual decrease in strength and a 1.2% loss in BMD at the total hip (96).

The menopausal transition in older women is associated with increased bone loss, hormonal fluctuations, and increased inflammation as a result of estrogen deficiency's impact on bone remodeling (57,127,128). Postmenopausal women with HIV are at an increased risk of osteoporosis and fractures due to factors such as low BMI, smoking, substance abuse, AIDS-defining illnesses, uncontrolled HIV infection, and the use of ART (70). HIV-infected individuals often experience decreased BMD, higher fracture rates of 30-70%, three-fold risk of osteoporosis, and seven-fold higher risk of osteopenia than non-HIV-infected individuals (29,102). HIV and menopause significantly impact BMD, with the association being more pronounced in postmenopausal women. A longitudinal study in urban South African women discovered that WWHIV transitioning through menopause experienced increased bone loss, particularly in rural areas (103–105), potentially due to a higher risk of premature menopause (115). The Women's Interagency HIV Study (WIHS) discovered that menopause independently predicts lower bone BMD, having an additive impact on lumbar spine and total hip BMD when coupled with HIV infection (133).

HIV-positive individuals are at a higher risk of developing osteoporosis, with the incidence rising with age, particularly due to the potential decline in BMD among menopausal women (100). Menopausal symptoms, such as mood swings, depression, and anxiety, can negatively affect women's psychological well-being, and socio-cultural factors in Sub-Saharan Africa can complicate mental health management. The onset of menopause also increases the risk of cardiovascular diseases, influenced by lifestyle, diet, and access to healthcare. Furthermore, there are racial differences in the risks of bone loss among middle-aged women, regardless of HIV status (102). HIV infection impacts bone mineral density differently in black and non-black women, with non-black women experiencing greater bone loss during menopause. Black women show a significant decrease in total hip BMD during this period. It is essential to understand the racial and ethnic disparities in osteoporosis and fracture risk, particularly among women living with HIV.



A longitudinal study involving Hispanic and African American women found that postmenopausal minority women living with HIV had lower BMD, higher bone turnover, and a greater incidence of bone loss compared to those without HIV (93). Recently, the medical and scientific communities have begun to examine the effects of HIV and menopause on BMD more closely(134). Multiple studies have demonstrated that HIV infection is associated with a reduction in BMD, leading to a higher prevalence of osteoporosis and osteopenia among individuals living with HIV—both conditions linked to low BMD (116,122,135,136). Chronic HIV infection and the use of antiretroviral therapy (ART) are connected to alterations in vitamin D metabolism, decreased BMD, and an increased risk of fractures (101,110,137). This reduction in BMD increases the risk of fractures and other bone-related complications, which can significantly impact the quality of life for those affected by HIV (91).

The decrease in BMD in HIV-infected individuals is believed to be largely due to inflammation and immune activation, which are common in people living with HIV. Additionally, ART, the standard treatment for managing HIV, has also been associated with bone loss. While ART has revolutionized the treatment of HIV, making it a manageable chronic condition, its impact on bone health represents one of its significant long-term side effects (93). The majority of research on bone health and HIV infection has been carried out in Europe and North America. It may not be appropriate to generalize these findings to other populations. Despite the limited data on fractures in Africa, studies carried out in resource-rich environments have consistently shown an association between HIV infection and low bone mineral density (BMD), along with an elevated risk of fractures (93).

Future research should explore racial and ethnic inequalities in menopausal symptoms, including symptom manifestation, associated comorbidities, HIV's impact on BMD and fracture risk in ageing WLHIV focusing on equitable healthcare access and management strategies to reduce osteoporosis and fracture risk (65,67,111,112). Moreover, despite the limited data on fractures and the impact of race on osteoporosis in Africa (92), studies in resource-rich populations have consistently shown an association between HIV and low BMD, along with an increased risk of fractures (102).

Cardiovascular Diseases

Menopause is associated with an increased risk of cardiovascular diseases (CVD), influenced by lifestyle, diet, and healthcare access (13). Additionally, vasomotor symptoms have been associated with a higher risk of CVD (53). This is particularly concerning for women living with HIV, as the virus and its treatments may worsen their cardiovascular risk. There is a significant lack of research on cardiovascular disease in menopausal WLHIV in Sub-Saharan Africa. Studies in North America and Europe have found an association between HIV infection and higher CVD risk in WLHIV (116), with some indicating a higher prevalence of cardiovascular events in HIV-positive women compared to



HIV-negative women (117–119). However, findings have been inconsistent, with some studies showing no significant relationship between CVD risk and HIV infection(120).

Obesity

In postmenopausal women in particular, the co-occurring conditions of obesity and HIV may act in combination to increase the risk of comorbidities such as diabetes, cardiovascular disease, and fatty liver disease (84). The health outcomes of individuals living with HIV are significantly impacted by weight gain, which has been associated with liver problems, kidney disease, and cardiovascular disease (86–88). Nonetheless, a prior study found lower BMI exhibited among postmenopausal women with HIV (85). Research has shown that within the HIV-positive population, obesity is more prevalent among individuals of black African ethnicity, showing a significant association, with African American women exhibiting higher BMIs compared to white women (88–90). It is unclear what factors contribute to obesity in women living with HIV who are black African and other black ethnicities (84). Despite these findings, no association was found between BMI and physical activity with the age at natural menopause (36). Furthermore, no correlation was found between BMI, physical activity levels, and the age at which women experience natural menopause. Although previous research indicates that women with lower BMI may undergo natural menopause earlier in life (145–147).

HIV

HIV and Menopause

Menopause is the primary risk factor for bone loss in middle-aged women. However, the rate of bone loss varies widely among different racial and ethnic groups, potentially affecting fracture rates across various demographics (87). Both HIV infection and menopause can significantly influence bone mineral density (BMD), raising the risk of osteoporosis and fractures in individuals impacted by these conditions (133,139).

The combined effects of menopause and HIV can have significant implications (7) as menopause may influence the progression of HIV infection itself (28). While menopause is the primary risk factor for bone loss in middle-aged women, the rate of bone loss varies considerably among different racial and ethnic groups, potentially affecting fracture rates across various demographics (87). Both HIV infection and menopause can significantly affect bone mineral density, increasing the risk of osteoporosis and fractures in individuals impacted by these conditions (133,139). Additionally, HIV infection may alter menopausal processes, resulting in earlier onset of menopause, more severe symptoms, and changes in reproductive hormone profiles in affected women (16).

WLHIV frequently experience a higher prevalence of physical and psychological symptoms(21), which may be associated with disease progression (10). Studies have shown that vasomotor



symptoms (VMS), which are more prevalent in HIV-positive women, are associated with an increased risk of HIV infection (53). Studies suggest that HIV-positive women are more prone to experiencing menopausal symptoms such as hot flushes (38), vasomotor symptoms (44,45) sexual dysfunction (44), and mood changes (45), while other reports found no correlation between HIV status and these symptoms, particularly hot flushes and vaginal dryness (46). According to recent reports, women with low CD4+ cell counts (i.e. CD4 cell count below 200 cells/mm³) show an increased risk of early onset of menopause (9,18). HIV-related immunodeficiency has been associated with an earlier onset of menopause. However, factors such as tobacco consumption, ART use, low CD4 count, high viral load, and AIDS progression were not (18). The Women's Interagency HIV Study indicates that HIV-positive women experience an increased risk of immune activation during menopause, with postmenopausal women displaying elevated levels of innate immune activation, primarily influenced by ovarian ageing (6).

Factors influencing HIV include the risk of acquisition and transmission, infection progression, and antiretroviral pharmacokinetics (28). Additionally, age-related interactions, cardiovascular health, bone mineral density, and cognitive function are also impacted by HIV infection. Furthermore, lifestyle and demographic factors significantly affect the relationship between HIV infection and menopause in HIV (16). Menopause can affect HIV prognosis, necessitating managing symptoms alongside HIV (28). Healthcare providers encounter challenges in treating women living with HIV, highlighting the need for a paradigm shift in their approach to care (28). HIV-positive women may experience improved health outcomes through effective immune reconstitution and optimal suppression of viral replication achieved through combination antiretroviral therapy to mitigate the effects of HIV-related factors on their overall health (58). HIV infection increases the risk of chronic amenorrhea without ovarian failure, emphasising the importance of tailored disease management in women with irregular menstruation and anovulation (58).

Menopause and HIV Treatment

The HIV pandemic has significantly evolved over the past three decades, largely due to the introduction of combination antiretroviral treatment (cART), which has substantially decreased HIV-related morbidity and mortality, resulting in remarkable advancements in HIV management. With access to effective cART, the life expectancy of newly diagnosed individuals has improved significantly, now similar to that of the general population. This advancement has transformed HIV into a manageable chronic illness, marking a significant milestone in medical progress (28,152). The transformation of HIV treatment from addressing an acute infection to managing it as a chronic illness with highly effective medications represents a significant medical achievement (5).

HIV and its treatment are associated with decreased BMD (40), leading to higher rates of osteopenia and osteoporosis among individuals with HIV (35,87–89). Factors contributing to low BMD include



viral, immune, inflammatory, and treatment-related effects. Women starting antiretroviral therapy (ART), particularly with tenofovir disoproxil fumarate (TDF), often experience significant reductions in BMD and an increased risk of osteoporosis (57,155). ART medications such as tenofovir (85) influence bone loss at the lumbar spine (LS), total hip, and cortical-rich sites (69,86). ART is associated with a 2%-6% decrease in BMD during the first two years of treatment (29), with women living with HIV showing a rising incidence of reduced BMD (34,82,84), typically one to two years after starting ART (115). While substantial bone loss can occur at the beginning of ART, this loss usually stabilizes with long-term treatment (122).

Multiple factors, including the effects of ART, contribute to bone loss in individuals with HIV. Upon the initiation of ART, there is a temporary rise in bone turnover, which results in bone loss (92,97). HIV infection is associated with risk factors such as ART and exposure to tenofovir in some studies, however, this was not consistent across all studies (93,98). Menopause can impact HIV treatment response by affecting estrogen synthesis, HIV replication, and the recovery of CD4 cells. Changes in age-related immune function, along with hormonal fluctuations, may also affect the response to ART in both premenopausal and postmenopausal women. Additionally, higher CD4 cell counts, and the use of ART may decrease amenorrhea in WLHIV (7). Studies show that menopausal status does not significantly affect treatment response to ART in women with HIV, as both premenopausal and postmenopausal women can attain virologic suppression (54). Postmenopausal women showed a lower median CD4 response compared to premenopausal women 24 months after starting ART, suggesting a complex relationship between HIV infection and menopause (9).

Challenges in Managing Menopause and HIV

The combined effects of HIV, aging, and menopause may elevate the risk of non-AIDS-related diseases and mortality among older women living with HIV. While the early onset of natural menopause was not significantly linked to the use of combination antiretroviral therapy (cART), severe immunosuppression (CD4 count <50 cells/mm³) and chronic hepatitis C virus (HCV) infection were significantly associated with early menopause (54). When addressing HIV, it is essential to consider factors such as the risk of acquisition and transmission, the progression of the infection, and the pharmacokinetics, effectiveness, and side effects of antiretroviral therapy. Although menopause may influence HIV prognosis, its symptoms and complications should be managed separately from those related to HIV (28). With the introduction of a more accessible and effective combination antiretroviral therapy (cART) and longer life expectancies, HIV in the context of ageing becomes a significant clinical consideration. Healthcare providers may lack knowledge about menopause treatment risks and benefits, requiring improved access to information, and enhanced clinician-GP connections to help women navigate menopause effectively (52). A retrospective case notes review of a monthly HIV menopause clinic found that most referrals came from HIV clinicians



rather than general practitioners (GPs), suggesting a lack of awareness about dedicated menopause services (111). A survey of UK GPs revealed that less than half felt confident managing menopause in HIV-positive women (113,114). This lack of confidence leads to women being shuttled between specialists and general practitioners (52).

Research on the progression of menopause and treatment in older women living with HIV (WLHIV) is important. Health policy frameworks should be established to address the unique needs of women regarding HIV testing and to enhance care for the increasing population of postmenopausal WLHIV. This includes ensuring that healthcare systems are equipped with the necessary structure and resources to meet the specific needs of WLHIV, overcome barriers, and improve access to care (7,160). The effects of ageing are critical in HIV care, particularly for women navigating age-related life transitions. Healthcare providers and researchers must focus on the intersection of HIV infection and menopause, promoting cultural sensitivity and active participation in research initiatives to enhance menopausal care in developing countries (22). Healthcare professionals need to adjust their approach to HIV care to accommodate the needs of the aging population (28). Current guidelines offer limited direction on hormone replacement therapy (HRT) for menopausal symptoms in WLHIV (109). Regular evaluations of menopausal status, symptoms, and HRT provision are essential for peri- and postmenopausal women, necessitating interdisciplinary collaboration among HIV specialists, gynaecologists, and mental health professionals (37). Additionally, women's underreporting of menopausal symptoms to their HIV clinicians may result in delays in symptom management, referrals, and follow-ups, often due to a lack of awareness and the stigma surrounding these discussions (114).

Racial and Ethnic Disparities

Racial and ethnic disparities exist among women living with HIV, with Black/African American and Hispanic/Latina women being disproportionately affected, compared to women of other races and ethnicities (162,163). HIV treatment disparities are especially prominent among women, with race and ethnicity significantly contributing to delays in starting treatment and early discontinuation (164). Understanding the effects of HIV on women and menopause could be valuable in efforts to comprehend and reduce the racial and ethnic disparities related to HIV (7). The growing population of HIV-positive individuals reaching old age requires effective management of HIV and a thorough understanding of the physiological and psychological processes associated with ageing (63). Age-related comorbidities and life events, such as menopause, introduce distinct challenges and are becoming a significant focus in HIV care (152).



Methods of measurement

Menopause symptoms

The Menopause Rating Scale (MRS) II is a widely recognized standardized and validated tool developed in the early 1990s used to assess the severity of menopausal symptoms, evaluate the impact on health-related quality of life (HRQoL) and compare changes before and after menopausal hormone replacement therapy among ageing women(165). It provides a structured self-administered scale approach, enabling healthcare providers to collect consistent and comparable data on menopausal symptoms across diverse populations under various circumstances. Its validity and reliability have been extensively researched and confirmed, making it a reliable tool for assessing the severity of menopausal symptoms and monitoring changes over time. The MRS underwent formal standardization following psychometric guidelines and has demonstrated high reliability through test-retest stability and consistency across different countries, confirming its applicability in global health research (165). Although it was first published in German, the MRS has gained global recognition and widespread use, being accessible in 10 different languages. The scale has undergone extensive validation, including a multinational survey involving nine countries across four continents, establishing its credibility and cross-cultural applicability. It has been translated into multiple languages and adapted for international use, allowing comparisons with other scales like the Kupperman Index and the SF-36 Quality of Life scale, thereby facilitating a comprehensive evaluation of health-related quality of life during menopause (165).

Validity and Reliability

Ensuring the validity and reliability of the MRS specifically in women living with HIV is crucial to accurately capturing menopausal symptoms within this demographic. Social desirability bias might occur from the questionnaire-based data collection method, specifically when it comes to adherence-related questions (Solomon et al., 2021). Compared to women without menopausal symptoms, it is unlikely that women experiencing significant menopausal symptoms would distort their adherence, or vice versa (Solomon et al., 2021). Although the MRS is tailored to menopausal experiences, studies evaluating the validity of the MRS tool have suggested that the questionnaire items are designed to address menopausal symptoms, the presence of HIV-related comorbidities may complicate symptom manifestation (165). For example, psychological symptoms might be influenced by factors other than menopause, highlighting the need for additional qualitative research on psychological well-being and engagement in HIV care among this population (63).

Multinational Validation and Applicability

A large multinational survey gathered information on hormonal treatment in women aged 40-70 years across nine countries and cultures (165). The study confirmed the MRS's reliability and validity, with



the internal structure found to be consistent across countries. However, high correlations between sub-scores and the total score suggest that the subscales are not fully independent in practice. Despite this, the methodological evidence supports the high quality of the MRS, as long as construct validation is completed. While the MRS has proven to be a reliable and valid tool in various settings, it's crucial to determine whether the MRS is culturally sensitive and relevant. Its applicability to African nations requires careful assessment through validation studies that consider cultural, linguistic, and contextual factors (165). Researchers and healthcare professionals should exercise caution and may need to adapt or validate tools to ensure their relevance and accuracy in diverse cultural settings. This approach will help provide a more accurate and comprehensive assessment of menopausal symptoms in women living with HIV, enhancing the understanding and management of their health-related quality of life (165).

Cultural Sensitivity and Adaptation

When considering the implementation of the Menopause Rating Scale (MRS) in African countries, it is essential to evaluate its validity and reliability for the specific population it aims to serve. This requires conducting studies to confirm that the tool accurately measures its intended outcomes and yields consistent results over time. Menopausal experiences can differ significantly across cultures, highlighting the need to assess the MRS's cultural sensitivity and relevance to the diverse populations within Africa. Attention must also be given to language and translation issues to ensure proper adaptation and sensitivity to local languages and cultures. Validation studies tailored to the African context are critical, involving the testing of the MRS on varied samples of women to evaluate its reliability and validity. Furthermore, comparing the MRS with existing validated tools in the region may provide valuable insights into its compatibility with local contexts. Thus, careful consideration and adaptation may be necessary to ensure the tool's effectiveness and accuracy in assessing menopausal symptoms in African nations (165). Standardized tools for collecting menopause data among women living with HIV (WLHIV) can enhance research quality and clinical care by enabling comparisons across studies and countries (70).

Quality of Life

The Health-Related Quality of Life (HR-QoL) is a comprehensive assessment of an individual's overall well-being, including their physical, social, and psychological indicators. Women living with HIV have lower HR-QoL and are more likely to experience depression and anxiety than women in the general population, according to research from Public Health England (20). Menopausal is known to have a negative impact on HR-QoL, with symptoms such as vasomotor and urogenital complications significantly associated with an adverse impact on overall quality of life. Menopause and Health-Related Quality of Life (HR-QoL) have a complex and dynamic relationship (20). Perimenopausal women—who may undergo elevated symptoms—are more likely to have a lower



HR-QoL, particularly if their symptoms prolong, compared to postmenopausal women. There is a lack of research evaluating the combined effects of menopausal status, symptoms, and HIV status on HR-QoL, despite the understanding that menopause impacts HR-QoL in the general population and that women with HIV have lower HR-QoL (20).

Bone Health

Dual X-ray absorptiometry (DXA) is an imaging method employed to assess bone mineral density (BMD), allowing for the early detection and prevention of fractures (109). In HIV-positive women, fracture risk assessment involves DXA evaluation of BMD, especially for postmenopausal women and those over 50 who exhibit clinical risk factors (101). The European AIDS Clinical Society (EACS) advises the use of DXA to assess spine and hip bone mineral density (BMD) in postmenopausal women living with HIV who are over 50 (122). The Fracture Risk Assessment Tool (FRAX) is recommended for women aged 40 and older. It is important to exclude other potential causes of osteoporosis in women with low BMD and to assess the risk of vertebral fractures in those with specific indicators (101).

In South Africa, the evaluation of bone health status is significantly restricted by the unavailability and high cost of specialized equipment necessary to measure bone mineral density. Studies show that trends in BMD in Africa might be consistent with findings from northern hemisphere countries; however, fracture rates appear to be significantly lower in this region (124). Dual-energy X-ray absorptiometry (DEXA) is considered the gold standard for determining BMD loss in the diagnosis and management of osteoporosis. Although DEXA has been recognized as the most efficient clinical tool for osteoporosis diagnosis, it does have limitations. Challenges in assessing BMD in certain populations derive from the unequal access to DEXA across various clinics and regions. employing this assessment method as a diagnostic and research tool for a specific population, it is essential to validate its use (124). Given the limited availability of DEXA in healthcare facilities, employing a range of diagnostic methods is crucial for comprehensive BMD assessment. It is essential to compare and validate alternative BMD measurement techniques using the DEXA T-score as the standard reference point. As such, in resource-constrained settings, other diagnostic assessment methods notably Quantitative Ultrasound (QUS) are used to measure BMD (124).

Osteoporosis management in HIV-positive patients does not vary significantly from that in HIV-negative patients. In women with HIV, recommendations for the prevention and management of osteoporosis involve routine FRAX screening, calcium and vitamin D supplementation, use of bisphosphonates as a therapeutic option, possible modifications to antiretroviral therapy to improve bone health, and consideration of hormone replacement therapy for ovarian insufficiency in women (95). In postmenopausal women living with HIV, proactive screening and personalized guidance are essential to address their increased susceptibility to bone-related conditions (95).



Menopause stages

The Stages of Reproductive Aging Workshop (STRAW), recognized as the gold standard for staging menopausal transition (MT), defined criteria in 2001 for each stage of reproductive ageing (167,168). STRAW divided the adult female lifespan into three primary phases: reproductive, menopausal transition, and post-menopause (167). Menopause was designated as Stage 0 of the STRAW criterion, which divided female reproductive ageing into seven separate stages based on the FMP. Five stages (-5 to -1) precede the FMP, followed by two stages after (+1 to +2) (23).

The reproductive phase includes early, peak, and late stages represented by Stages -5, -4, and -3, respectively. The onset of menstrual cycle changes and increased follicle-stimulating hormone (FSH) levels are the first indicators of the menopausal transition phase, which encompasses Stages -2 (early) and -1 (late), ending with the FMP. Stages +1 (early) and +2 (late) constitute the post-menopause phase. Early post-menopause (+1) is defined as occurring within 5 years of the FMP and is further divided into 'a' (the first 12 months) and 'b' (the following 4 years). Late post-menopause (+2) continues until a woman's death and perimenopause (-2 to +1a) ends 12 months after the FMP (168). (23) STRAW and STRAW+10 do not define premenopause explicitly, however, it should be precisely defined and transparently reported (23,34,167).

Stage -3 is characterized by regular menstrual cycles and rising FSH levels, while Stage -2 is marked by irregular menstrual cycles and elevated FSH levels. The onset of skipped cycles or amenorrhea lasting at least 60 days, along with a consistent increase in FSH, defines Stage -1 (167). Increased variability in menstrual cycle length indicates the early menopausal transition (Stage -2), whereas an amenorrhea period of 60 days or more, combined with FSH levels exceeding 25 IU/L, signifies the late menopausal transition (Stage -1). The early post-menopause is divided into three stages (+1a, +1b, and +1c), reflecting changes in FSH and estradiol levels over the two years following the FMP. Stage +1a marks the conclusion of perimenopause, occurring 12 months after the FMP, while Stage +1b represents the year leading up to the stabilization of elevated FSH and decreased estradiol levels, which culminates in Stage +1c (35,167). The STRAW +10 staging system, which outlines each phase of the menopause transition, is illustrated in [Figure 2](#).



	Final Menstrual Period (FMP)							
<i>Stages:</i>	-5	-4	-3	-2	-1	0	+1	+2
<i>Terminology:</i>	Reproductive			Menopausal Transition		Postmenopause		
	Early	Peak	Late	Early	Late*	Early*	Late	
				Perimenopause				
<i>Duration of Stage:</i>	variable			variable		a 1 yr	b 4 yrs	until demise
<i>Menstrual Cycles:</i>	variable to regular	regular		variable cycle length (>7 days different from normal)	≥2 skipped cycles and an interval of amenorrhea (≥60 days)	none		
<i>Endocrine:</i>	normal FSH		↑ FSH	↑ FSH		↑ FSH		

**Stages most likely to be characterized by vasomotor symptoms ↑ = elevated*

Figure 2: The STRAW staging system (135).

Adaptations and Limitations

Although the validity and reliability of the original STRAW guidelines have been evaluated and have received widespread support from international cohort studies such as the Study of Women's Health Across the Nation (SWAN), limitations have been recognized that have led to recommendations for adjusting the STRAW criteria (35,169).

The original STRAW criteria focused primarily on FSH as a biomarker, highlighting menstrual bleeding patterns and qualitative FSH levels (23). However, due to a lack of data, the criteria did not provide much information on the precise timing of changes in FSH levels or quantitative FSH requirements (167). Anti-Mullerian hormone (AMH) has been considered an ideal option as an international standard biomarker, given its stability in against hormonal changes, including sudden increases in FSH and estrogen hormones (170–173). Follicle-stimulating hormone (FSH) levels were suggested by the 2001 STRAW recommendation to be used as supportive criteria to confirm the stage of the Menopausal Transition (MT), with FSH functioning as a biomarker in the late transition stage, particularly before and after the Final Menstrual Period (FMP) (53,168). Menstrual cycles remain an important factor in determining the Menopausal Transition (MT) stage due to the absence of clear criteria for biomarker testing. A lack of resources in low- and middle-income nations prevents the widespread use of blood tests for determining the stages of the reproductive cycle (53).

The STRAW guidelines had certain limitations, as they recommended that the staging system be applicable only to healthy women. Women using exogenous hormones, such as hormone replacement therapy (HRT), were deemed ineligible. Furthermore, the guidelines advised against applying the criteria to women with specific medical conditions, including those who had undergone



a hysterectomy, experienced chronic menstrual irregularities, had uterine abnormalities (e.g., fibroids), ovarian anomalies (e.g., endometriomas), significant illnesses like cancer, or were classified as obese (BMI > 30 kg/m²) and smokers (23,167).

The initial limitations of the STRAW criteria in being applicable to various populations were attributed to the lack of data from multiethnic cohorts or different socioeconomic groups during its development (167). Additionally, the initial STRAW criteria focused solely follicle-stimulating hormone (FSH) as a biomarker, lacking specific guidance on the timing of FSH level changes and quantitative FSH criteria due to data insufficiency. Consequently, the initial STRAW criteria emphasized menstrual patterns and qualitative FSH levels. However, in resource-limited settings, the STRAW+10 staging system is found to be appropriate for staging menopause, relying on self-reported bleeding criteria and emphasizing validated interviewer inquiries and precise technical terminology to enhance accuracy (53).

In 2011, the STRAW+10 criteria were developed to overcome these limitations, enhancing the staging system by dividing the late reproductive stage (-3) into two stages (-3b and -3a) based on menstrual cycle characteristics and FSH levels. This improvement sought to identify subtle changes in menstrual cycle patterns, such as shorter cycle lengths in stage -3a, and increased variations in FSH levels (167). Later, the STRAW+10 criteria identified menstrual cycle variability as the primary criterion for the reproductive staging system (23), emphasizing precise menstrual cycle criteria and the quantification of FSH levels during the late menopausal transition (167). Additionally, the updated recommendations highlighted the significance of accurate menstrual cycle criteria for distinguishing the early (-2) and late (-1) menopausal transition stages, as well as the quantification of FSH levels during the late menopausal transition (35,167).

Although there were limitations, the STRAW+10 criteria have made a substantial contribution towards our understanding of women's health, receiving acknowledgment as the gold standard for defining terms related to female reproductive aging, and have shown to be broadly applicable across diverse populations and lifestyles. Further research is essential to standardize tests for biomarkers like AMH and to enhance our understanding of reproductive aging in women with specific medical histories, such as HIV infection or cancer treatment (23,167).

Management of Menopause in WLHIV

Hormone replacement therapy

Hormone replacement treatment (HRT) has been shown to be advantageous in women living with HIV for the prevention of osteoporosis, cardiovascular disease (CVD), and management of symptoms associated with perimenopause (174).



Menopause significantly impacts women's health and overall well-being, although limited research has been conducted on how menopause affects women with HIV, particularly concerning the severity of menopausal symptoms (175). The complicated and poorly understood association between menopause and HIV infection poses significant problems for healthcare practitioners in managing older HIV-positive women (5). Compared to women in the Netherlands with higher awareness and milder symptoms, rural Xhosa women experiencing similar menopausal symptoms, showed significantly lower awareness of available treatment options such as hormonal therapy, with majority (94%) having no prior knowledge of this treatment (13). Several factors are associated with HIV, including the risks of acquisition and transmission, the progression of the disease, variations in the dynamics and effectiveness of antiretroviral therapy, and possible adverse effects. The management of menopausal symptoms and challenges should be integrated with HIV care, considering the increasing significance of HIV treatment in the context of age-related health issues and life transitions, such as menopause (28).

Menopause management for women living with HIV (WLHIV) is primarily handled in primary care centers in the United Kingdom. However, primary care physicians often lack experience in managing the comorbidities and medication interactions in this population (11). Conversely, healthcare professionals specializing in HIV treatment may not be competent in treating menopausal symptoms. While the inclusion of clinics providing both menopausal and HIV treatment is a step forward, these services are rare in the UK (11). Less than half of primary care practitioners in the UK feel confident managing menopause in WLHIV, in contrast to the high confidence levels in managing menopause in HIV-negative women. Many respondents believe that menopause in WLHIV should be managed in primary care, though almost all agree that menopause in HIV-negative women should be handled similarly (159).

There is currently no European guideline addressing the screening and management of age-related comorbidities and events in WLHIV, despite the rising number of older women living with HIV continues and their higher risk of comorbidities and menopause-related symptoms. Moreover, there is limited understanding of how this demographic is cared for in Europe (176). Menopausal symptoms significantly affect patient engagement with healthcare (63). Healthcare providers who acknowledge the limited understanding of menopause and initiate conversations with their patients may be better equipped to manage menopausal symptoms effectively (58). To assist primary and secondary care physicians in identifying WLHIV who are exhibiting menopausal symptoms and ensuring that they receive adequate treatment and care, integrated clinical pathways should be established (63). Specialized protocols for menopause care in WLHIV are considered advantageous. Clinical services, training programs, specialized guidelines on HIV and menopause, and clear care paths for tertiary referrals are essential to improving care for WLHIV transitioning through menopause (11).



Antiretroviral Therapy

Highly active antiretroviral therapy (HAART) has significantly reduced morbidity and mortality rates associated with HIV (177). In menopausal women living with HIV (WLWH), increased depression symptoms are linked to decreased adherence to antiretroviral therapy (ART), though research on the overall impact of menopausal symptom severity on ART adherence is limited (71). It is important to assess drug-drug interactions and comorbidities when considering ART, as these factors can affect treatment efficacy. Healthcare professionals must be prepared to address the evolving needs of people living with HIV (PLWHIV) (152).

Menopausal symptoms can adversely affect ART adherence, adding complexity to the management of perimenopausal women with HIV (61–63). Women with HIV may confuse menopausal symptoms with ART side effects or other medical conditions. Distinguishing between menopausal symptoms and HIV or ART side effects presents a challenge for WLHIV and their healthcare providers, leading to poor ART treatment adherence and worsened HIV-related outcomes (175). Early perimenopause is often when menopausal symptoms are evident (175). The effect of the menopause transition on women's engagement in HIV care is still barely understood, despite the clinical necessity (63). Treating these symptoms is crucial to improve the quality of life for peri- and menopausal WLHIV and to enhance ART adherence (175).

Menopausal hormone treatment (MHT) has been effective in treating menopausal symptoms (178). Studies indicate that WLHIV use hormone replacement therapy (HRT) less frequently than HIV-negative women, despite experiencing higher rates of vasomotor, urogenital, and psychological symptoms. Severe menopausal symptoms have been associated with poor ART adherence and increased HIV risks (63).

Severe menopausal symptoms can complicate HIV management, negatively impacting the health and well-being of WLHIV. Suboptimal attendance at HIV clinics has been associated with significant somatic and psychological symptoms, suggesting these factors contribute to poor clinic visits and ART adherence (63). Although causation cannot be established, severe menopausal symptoms are significantly associated with suboptimal ART adherence and HIV clinic attendance, highlighting the need for longitudinal studies. Studies in other populations have indicated an association between psychological distress and clinic attendance (179). Research in various geographic contexts, where cultural norms and healthcare availability differ, is essential to understand the impact of menopausal symptoms on HIV care utilization (63).



Menopause and HIV

HIV and Menopause: A Complex Intersection

The intersection of menopause and HIV presents a unique and underexplored challenge for women in Sub-Saharan Africa, where both the prevalence of HIV and the aging population are on the rise (5). HIV and menopause pose a unique challenge that adds layers of complication to the menopausal experience, which is inherently complex. Understanding the interplay between menopause and HIV in this region is crucial for developing tailored interventions that address the specific needs and challenges faced by this vulnerable population(60,180). People living with HIV (PLWHIV) are more prone to liver disease, renal dysfunction, cardiovascular issues, diabetes mellitus, cancer, fractures, and cognitive impairment compared to the non-infected population, often manifesting at an earlier age(181). Compared to their HIV-negative counterparts, WLHIV frequently experience menopause earlier in life (52,161,182). The primary cause of this phenomenon is the negative impact of HIV on ovarian function, resulting in an early reduction of ovarian follicles (8,25,183). Additionally, an array of severe symptoms often corresponds with menopause in women living with HIV(15,149). Compared to women who are HIV-negative, women with HIV often report more severe menopausal symptoms, such as hot flushes, mood swings, physical/mental exhaustion, joint and muscle dysfunction, sexual dysfunction, and difficulty sleeping, which significantly lower their overall quality of life (4,20,58,61,64,70,184). Menopausal transition is associated with mood swings and sexual dysfunction, both of which can lower women's quality of life(81,180,185). Long-term menopause accelerates the progression and onset of aging-related chronic illnesses, such as diabetes, high blood pressure, heart disease, and lowered bone mineral density (124,186–188). Factors such as race/ethnicity, education level, monthly family income, parity, oral contraceptive usage, alcohol and cocaine consumption, body mass index (BMI), type 2 diabetes, hypothyroidism, and cART use were not significant predictors of earlier age at natural menopause (52,54,161). Other factors associated with an earlier onset of natural menopause included early menarche, cigarette smoking during the study period, chronic hepatitis C virus (HCV) infection, and severe immunosuppression (29,36,183). Furthermore, a study demonstrated that postmenopausal women, among HIV-uninfected individuals, have lower CD4 cell counts compared to premenopausal women. This raises the question of whether a low CD4 cell count increases the risk of early menopause(189). If so, the compounding effects of HIV infection and menopause could have significant consequences.

HIV in Sub-Saharan Africa

The HIV pandemic in Sub-Saharan Africa, particularly Southern Africa, accounts for over 60% of global HIV infections, disproportionately affecting urban adolescent girls (190). HIV-positive women face a multitude of challenges that negatively impact their quality of life, including financial difficulties, social issues, mental health disorders, and gender-based violence (20). Understanding the



physiological and psychological factors of ageing in WLHIV in the context of menopause is necessary (63).

Due to the scarcity and high cost of specialized equipment for determining BMD, bone status is almost non-existent in South Africa (124). A few studies revealed that while BMD in Africa might be comparable to measurements in the north, the incidence of fractures seems to be significantly lower (124). Longitudinal studies are scarce within Sub-Saharan Africa, with only a few studies examining the relationship between HIV and menopause on bone health in the Sub-Saharan African population (139). A smaller two-year longitudinal study of South African postmenopausal women living with HIV on ART showed little change in BMD, potentially due to the small sample size and short follow-up period (191). The effects of menopausal transition on bone health have been thoroughly documented in North America and other high-income countries; however, there is a scarcity of data from Sub-Saharan Africa (138). In Ethiopia, there is a lack of published studies on the experience of perimenopause. Most menopause research has focused on Caucasian women from high-income countries, potentially impacting symptom reporting in international studies(15). There is a significant gap in the literature concerning women living with HIV in Sub-Saharan Africa, highlighting the need for more research, particularly longitudinal studies, to evaluate fracture incidence and the effects of HIV on postmenopausal women in South Africa (138).

Furthermore, a scarcity of information about menopause health and resources for managing menopausal symptoms leaves women ill-equipped to handle this stage of their lives (192). HIV not only precipitates the onset of menopause but also intensifies its symptoms (70). These experiences vary considerably across different global contexts, with women in Sub-Saharan Africa facing particularly daunting challenges due to socio-cultural barriers and limited healthcare access (192).

Existing Knowledge in the Field:

Menopause is an important factor in the aging process for women who are HIV positive, who now constitute over half of the HIV-positive population worldwide (152). As WLHIV are living longer, the aging process and its related symptoms have emerged as significant concerns in HIV care (152). The menopausal experiences of women living with HIV are not universal and vary significantly depending on the geographical context (60). Women living with HIV have been found to manage menopausal symptoms more effectively in developed countries, where healthcare and support services are more accessible (20). This is largely due to their access to advanced medical treatments and comprehensive healthcare plans, which have made it easier for many women to adapt to menopause (20,72). In less developed countries, the reality is considerably different. The stigma surrounding HIV, combined with limited access to healthcare often makes menopause more challenging for women (193).



Existing literature on menopause in women living with HIV in Sub-Saharan Africa is limited, with the majority of available data collected in North American and European contexts (65). Despite the increasing global population of aging women, there has been limited research on menopausal women in low- and middle-income countries (15). The limited research on the effects of menopause on the lives of women living with HIV (WLHIV), particularly in the Sub-Saharan African context, where cultural, social, and economic factors may further complicate their experiences (10). Furthermore, there are knowledge gaps regarding the relationship between HIV and menopause, particularly concerning the effects of menopause on cardiovascular, psychological, and bone health outcomes in WLHIV (22).

Although significant research has been carried out on menopause in Western populations, the menopausal experiences of African women are still relatively underexplored (177), as menopause research has predominantly centered on white middle-class women in high-income countries (9). Research from the UK highlights the insufficient attention given to African women during this period, especially concerning the relationship between HIV infection and menopause (195). A study conducted on perimenopausal women in Ethiopia highlighted a lack of understanding regarding the relationship between menopausal experiences and factors such as ethnicity, country of origin, and social constructs (15). For women living with HIV in Zimbabwe and other Sub-Saharan African regions, there is an urgent need for increased understanding on menopausal health. Implementing findings from high-income countries is unsuitable due to cultural variations, disparities in health-seeking habits, and access to menopausal care (58).

Tailored healthcare interventions should address sociodemographic factors affecting menopausal symptoms and experiences in Sub-Saharan Africa (109). Women experiencing severe menopausal symptoms not only have a diminished quality of life but also exhibit lower engagement in medical care and adherence to their ART (77,110). A comprehensive clinical approach addressing menopausal symptoms can enhance adherence to antiretroviral therapy (ART) and clinic attendance in midlife HIV-positive women, thereby reducing disparities in care and clinical outcomes (110). Comprehensive menopause management strategies for HIV-positive women require tailored interventions, support, training, and collaboration between HIV services and primary care to address disparities (52).

Although numerous epidemiological studies have advanced our understanding of menopause and HIV separately, there has been limited research on their combined effects in the Sub-Saharan African context. The few empirical studies available provide limited insights into the complex epidemiological factors that shape the menopausal experiences of women living with HIV (WLHIV) in this region (65).



4. Research Gap

Menopause and HIV present unique challenges for women living with HIV (WLHIV) in Sub-Saharan Africa (SSA), where HIV prevalence is high and access to healthcare resources may be limited. Despite significant advancements in HIV treatment and care, there is a lack of research specifically addressing the menopausal experiences of WLHIV in SSA.

Existing studies on menopause often fail to consider the compounded effects of living with HIV, specifically for aging women undergoing menopause. There is limited understanding of the impact of HIV-related, physiological, psychological, and socio-economic factors on the menopausal experiences and health outcomes of women facing both menopause and HIV. Additionally, there is a lack of comprehensive epidemiological data on the prevalence and onset of menopause among WLHIV in SSA, the association between HIV and menopause, and the specific menopausal symptoms experienced by WLHIV in SSA. Further study exploring the significance of menopause and HIV in Sub-Saharan Africa, and the unique challenges encountered by WLHIV in this context is required (14).

Addressing these research gaps can contribute to a more comprehensive understanding of the complex association between menopause and HIV in Sub-Saharan Africa, providing valuable insights into developing effective healthcare interventions and services for managing menopause among WLHIV.

5. Rationale

Sub-Saharan Africa has the highest global prevalence of HIV, with a considerable number of those affected being women. The challenges of managing menopause for Women Living with HIV (WLHIV) are intensified by socioeconomic disparities and limited access to healthcare in this region. As advancements in antiretroviral therapy (ART) lead to increased life expectancy, the WLHIV population is aging, resulting in more women experiencing menopause and facing associated health challenges, including heightened risks for conditions like cardiovascular disease and osteoporosis. Menopause is experienced differently by WLHIV compared to the general population, often manifesting as more severe symptoms. Despite significant progress in HIV treatment and care, there remains a substantial gap in understanding the impact of HIV on the health of menopausal women in Sub-Saharan Africa (5).

A scoping review provides a comprehensive overview for exploring the complex relationship between menopause and HIV in Sub-Saharan Africa by summarizing the current limited body of evidence, identifying research gaps, highlighting key themes and enabling the synthesis of various studies (196–199), which may not be suitable for a more focused systematic review (200).



Significance of the Study:

This scoping review protocol addresses a critical epidemiological gap in existing literature. The findings will contribute to public health knowledge of the complex relationship between HIV and menopause by providing insights for future research into the challenges faced by women living with HIV during menopause. Understanding the menopausal experiences of WLHIV can guide the development of targeted health interventions and inform policy, ultimately improving health outcomes and quality of life of women living with HIV in Sub-Saharan Africa.

6. Aim

This scoping review aims to comprehensively explore the current literature on menopause experiences among women living with HIV in Sub-Saharan Africa to offer recommendations for future research and health interventions tailored to this population.

7. Objectives

The primary objective of this scoping review is to map out existing literature on the menopause experiences of WLHIV in Sub-Saharan Africa.

The secondary objective of this scoping review is to identify knowledge gaps and key themes in current literature that address the menopause experiences among WLHIV in Sub-Saharan Africa.

8. Research Question

The main research question was developed in accordance with our research aim using the PCC (Population, Concept, Context) framework following the JBI guidelines and suggestions for conducting a scoping review as outlined by (196) for formulating scoping review questions: "What is the current scientific understanding of the menopausal experiences among women living with HIV in Sub-Saharan Africa?"

The scope of this review will additionally consider the following related research questions:

1. How do women living with HIV experience menopause compared to women living without HIV in Sub-Saharan Africa, and how do these experiences compare globally?
2. What are the common menopausal symptoms experienced by women living with HIV compared to women living without HIV?
3. What gaps exist in the current literature regarding menopause experiences in women living with HIV in Sub-Saharan Africa, and what areas require further research and exploration?
4. How is menopause defined in studies and how are menopausal symptoms measured in women living with HIV?
5. What methodological approaches are used in existing studies to address the menopause experiences among WLHIV in Sub-Saharan Africa?



Our scoping review will be conducted from August 2023 and is expected to be completed by December 2023 to address these research questions.

9. Keywords

Menopause, HIV, Women living with HIV, Sub-Saharan Africa

10. Methods

This protocol was developed using the Joanna Briggs Institute (JBI) methodology framework for conducting scoping reviews (201,202) and in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses for Scoping Reviews (PRISMA-ScR) guidelines (PRISMA Checklist) (198).

We will follow a six-step framework (203). These steps consist of (1) formulating the research question, (2) identifying relevant studies, (3) selecting studies for inclusion, (4) charting data, (5) collating, summarizing, and reporting results, and (6) consultation (optional) (204).

Study design

This research will be conducted as a scoping review. Scoping reviews map available evidence in existing literature, evaluate research methodologies and identify knowledge gaps in a specific topic. The methodology of a scoping review enables the systematic search, iterative screening, synthesis and analysis of existing literature and accommodates the heterogeneity of study types and results (196,199,200,205).

Types of Sources

A literature search of the following bibliographic databases—PubMed and Science Direct—will be conducted to find relevant articles. We will additionally make use of Google Scholar. Sources of unpublished, non-peer-reviewed or grey literature will not be included as this would introduce the risk of publication bias and a lack of validity. To find further relevant studies, a manual search of the reference lists of selected articles to inspect citations of relevant studies meeting the inclusion criteria will be undertaken.

11.1 Eligibility Criteria

This scoping review will include original, peer-reviewed research articles, including studies published in English. There will be no time restrictions on publication dates to ensure the inclusion of a wider range of potential literature, although priority will be given to current literature to ensure relevancy.



This review will consider empirical research in observational study designs to gain a comprehensive understanding of the topic. Inclusion criteria comprise cohort, longitudinal, case-control, case series and cross-sectional studies. Exclusion criteria include editorials, commentaries, websites and book sections, encyclopedias, conference abstracts, book reviews, discussions or communications. Qualitative studies, systematic reviews, scoping reviews, reviews and meta-analyses will not be considered. The inclusion criteria will be based on our research aims and questions. We will report the inclusion criteria by using the recommended JBI 'Population, Concept, Context (PCC)' framework for scoping reviews (201).

The eligibility criteria will be applied consistently and independently by one reviewer during the study selection process. Any discrepancies will be resolved through discussion or consultation with the supervisor. The search strategy will be developed and enhanced by the primary reviewer, with a final review from the supervisor. Full scoping review eligibility criteria are described in [Table 2](#).

Population

Inclusion Criteria: Studies on perimenopausal and postmenopausal WLHIV in Sub-Saharan Africa will be included.

Exclusion Criteria: Studies on premenopausal women, women living without HIV in Sub-Saharan Africa, non-menopausal women, men, pregnant women, breastfeeding women, women under the age of <18, women who underwent hysterectomy will be excluded.

Concept

The eligibility criteria for this scoping review will consider all relevant studies on menopause experiences among women living with HIV (WLHIV) in Sub-Saharan Africa and any related topics. Studies unrelated to menopause will not be considered.

Context

Studies conducted in Sub-Saharan Africa or according to the Sub-Saharan context will be eligible. Studies conducted outside Sub-Saharan Africa will be excluded.

Table 2: Inclusion and exclusion criteria for included studies

	Inclusion criteria	Exclusion criteria
Population	Studies including perimenopausal and postmenopausal women living with HIV in Sub-Saharan Africa	Studies including premenopausal women, women living without HIV in Sub-Saharan Africa, men, non-menopausal women, pregnant women, women under the age of 18, breastfeeding women, and women who had undergone hysterectomy



Concept	Studies including relevant information on menopause	Studies not addressing menopause or unrelated to menopause (i.e. irrelevant information)
Context	Studies conducted within Sub-Saharan Africa	Studies conducted outside of the Sub-Saharan region (i.e. Europe, North America, Asia)
Study type	Original peer-reviewed research articles, Quantitative studies, Empirical research, Observational studies i.e. cohort, longitudinal, case-control, case series and cross-sectional studies Published in English, Human species	Non-peer-reviewed articles, Qualitative, mixed-methods studies, reviews (i.e. scoping reviews, systematic reviews, meta-analyses), conference abstracts, editorials, websites, book sections, encyclopedia, conference abstracts, book reviews, discussions, communications, supplements, commentaries, case reports, theses, and conference papers.
Publication date	No time restriction on publication date	None
Language	Studies published in English	Studies published in languages other than English

11.2 Search Strategy

The search strategy for this scoping review will be developed in accordance with the Population-Concept-Context (PCC) concept according to JBI guidelines for scoping reviews (201) and in collaboration with the supervisor. A senior librarian will be consulted to ensure the selection of relevant keywords. The search strategy will be conducted across each database mentioned above, with adjustments tailored to each database using keyword combinations of Medical Subject Headings (MeSH) terms and Boolean operator strategies “AND” “OR” and “ “ for phrases related to menopause, HIV, and Sub-Saharan Africa (see [Appendix I: Search Strategy](#)).

11.3 Study selection

Study screening and selection will be performed using Covidence as it facilitates title and abstract screening, and full text review of articles. The search results will be imported into Covidence, an online tool for conducting systematic and scoping reviews. Reasons for exclusion of full-text studies that do not meet inclusion criteria will be recorded and reported in the scoping review.

The study selection process will consist of two phases: screening the title and abstract of selected articles based on inclusion and exclusion criteria and reviewing the full texts for further assessment. The rationale behind the exclusion of evidence sources will be documented and reported. All identified citations will be collated and uploaded into Mendeley cite software. Screening of titles and abstracts will be performed iteratively and independently by one reviewer, with conflicts resolved



through discussion or consultation with the supervisor. The inclusion criteria will be reported using the 'Population, Concept of interest, Context (PCC)' framework recommended by the JBI for scoping reviews (201). Study results and inclusion process will be reported in the final scoping review and presented in a Preferred Reporting Items for Systematic Reviews and Meta-analyses extension for scoping review (PRISMA-ScR) flow diagram (see [Appendix II: PRISMA 2020 Flow Diagram](#)) (198).

The final search results will be exported from data sources and references will be imported into Covidence, an online citation screening and data extraction tool for systematic & scoping review management. The user-friendly interface facilitates efficient screening, data extraction, and quality assessment of included studies. This software will be utilized for the management of literature, screening titles and abstracts, and full texts of eligible articles. Detected duplicates will be automatically removed through the software's citation manager, along with individual inspection of authors' names and study titles across all literature sources and electronic databases to further ensure the elimination of any duplicates.

Quality Appraisal

This scoping review did not require a risk of bias assessment or critical appraisal tool. In accordance with scoping review criteria, the review did not evaluate the included articles' methodological quality. Critical appraisal or risk of bias assessment is often not recommended, as the primary objective of scoping reviews is to map existing evidence. An evaluation of the methodological limitations or risk of bias in the included studies is generally not conducted (201).

12. Data Extraction

The data extraction process for this study will follow the Joanna Briggs Institute's template for scoping reviews (201) to create a table summarizing evidence on the menopausal experiences of women living with HIV in Sub-Saharan Africa. The data extraction table will undergo an initial evaluation using three studies to ensure reliability and consistency. The data extraction process will be performed by one reviewer in an iterative process, reviewing the template after three studies are extracted to assess whether all relevant data are represented, or adjustments are required (206). The primary data extraction tool will be subject to additional changes and revisions as needed until the final extraction is completed, with any discrepancies resolved through discussion with the primary supervisor. Any adjustments will be clearly specified in the scoping review (206).

Study characteristics such as title, author(s), year of publication, study location, study design, study population (including inclusion & exclusion criteria), sample size, aims/objectives, study design, methodology, outcome measures, important results (199) menopause definitions, and major findings related to menopause experiences among women living with HIV (WLHIV) in Sub-Saharan Africa, will be extracted.



The Covidence data extraction template will be used to extract study characteristics and outcome data from included research articles, although adjustments will be made to suit the scoping review aims and outcomes. The final data will be imported into Spreadsheet Excel for analysis and summarization, enhancing the reliability and reproducibility of data extraction. However, authors of the included studies will not be contacted if relevant missing or additional data are required due to study resource restrictions and feasibility.

13.Data Presentation

The extracted data from included studies will be summarized and presented in a tabular format that aligns with the objective(s) and aim of our review (206) as shown in **Table 3**. A coherent narrative summary will accompany the tabulated and/or charted results, describing how the findings relate to the scoping review research question(s) and objective(s). Included studies will be categorized based on identified common themes as well as study locations, sample sizes, years of publication, type of methods used and study designs. The reporting of results may be refined towards the conclusion of the review as the reviewer becomes more familiar with the contents of the included studies (207).

Table 3: Data extraction methodology for included studies (199).

Category:	Description:
Study information	• Author(s) • Title • Study location • Year (publication date) • Objective(s)/Aim(s) • Study design
Participants	• Study population (inclusion & exclusion criteria) • Sample size
Implementation	• Methodology • Measures • Definitions used (i.e. theoretical framework) • Outcomes (if applicable)
Results	• Main findings

14.Project Tools

- i. Covidence (208)
- ii. Mendeley reference manager (209)

15.Research Team Member Roles

The scoping review protocol will have a single reviewer responsible for screening titles, abstracts, and full-text articles, as well as conducting data extraction and quality assessment. The reviewer will collaborate with a senior librarian for search strategy development and adhere to predefined inclusion and exclusion criteria. Any uncertainties or ambiguities will be documented. However, bias



and error chances may not be eliminated, which may be a limitation. This approach was chosen based on resource constraints and feasibility considerations for the scoping review protocol.

16. Ethical considerations

This paper does not require ethical approval as it synthesizes findings from existing research without creating new data or involving human participants. Ethical guidelines will be upheld during the review process, with appropriate citation and attribution of sources.

17. Expected Outcomes

The review aims to provide a comprehensive understanding of menopause experiences among women with WLHIV in Sub-Saharan Africa, identifying gaps in existing literature and offering insights for future research and interventions. The purpose of this review is to improve interventions and strategies for enhancing the overall well-being of WLHIV in the region, contributing to better healthcare outcomes and tailored support for this specific population.

18. Conclusions

This scoping review will contribute valuable insights into the association between menopause and HIV among women in Sub-Saharan Africa. The review will analyze existing literature to understand the challenges faced by WLHIV during menopause, provide a foundation for future research and contribute to the development of targeted interventions to improve the overall health and well-being of WLHIV in this region.

20. Acknowledgements

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Cochrane Public Health Group. (2011) Guide for developing a Cochrane protocol. Retrieved from:

http://ph.cochrane.org/sites/ph.cochrane.org/files/uploads/Guide%20for%20PH%20protocol_Nov%202011_final%20for%20website.pdf.

Dartmouth Biomedical Libraries. (2012). Systematic Review Steps. Retrieved from

<http://www.dartmouth.edu/~library/biomed/services/lgr/docs/SR-Steps-Roles-revised.docx>

Durham University Community. (2009). Template for a Systematic Literature Review Protocol. Retrieved from <https://community.dur.ac.uk/ebse/resources/templates/SLRTemplate.pdf>.

Warwick Medical School. (n.d.) Protocol Template: Systematic Review. Retrieved from

http://www2.warwick.ac.uk/fac/med/staff/bridle/sr/protocol_template.doc.

World Health Organization. (2011). Review Protocol Template. Retrieved from

http://www.who.int/hrh/education/Rec1_CPDforfacultyteachingstaff.pdf.



20. References:

1. The World Health Organization (WHO). The World Health Organization (WHO). 2023 [cited 2024 Aug 17]. HIV statistics, globally and by WHO region. Available from: <https://cdn.who.int/media/docs/default-source/hq-hiv-hepatitis-and-stis-library/j0294-who-hiv-epi-factsheet-v7.pdf>
2. UNAIDS. UNAIDS. 2024 [cited 2024 Aug 17]. Global HIV & AIDS statistics — Fact sheet. Available from: <https://www.unaids.org/en/resources/fact-sheet>
3. Nelson HD. Menopause. *Lancet*. 2008 Mar 1;371(9614):760–70.
4. Woods NF, Mitchell ES. Symptoms during the perimenopause: prevalence, severity, trajectory, and significance in women's lives. *Am J Med*. 2005 Dec 19;118 Suppl 12B:14–24.
5. Andany N, Kennedy VL, Aden M, Loutfy M. Perspectives on menopause and women with HIV. *Int J Womens Health*. 2016;8:1–22.
6. Peters BA, Xue X, Sheira LA, Qi Q, Sharma A, Santoro N, et al. Menopause Is Associated With Immune Activation in Women With HIV. *J Infect Dis*. 2022 Jan 18;225(2):295–305.
7. Imai K, Sutton MY, Mdodo R, del Rio C. HIV and Menopause: A Systematic Review of the Effects of HIV Infection on Age at Menopause and the Effects of Menopause on Response to Antiretroviral Therapy. *Obstet Gynecol Int*. 2013;2013:1–11.
8. Cejtin HE, Kalinowski A, Bacchetti P, Taylor RN, Watts DH, Kim S, et al. Effects of human immunodeficiency virus on protracted amenorrhea and ovarian dysfunction. *Obstetrics and gynecology*. 2006 Dec;108(6):1423–31.
9. Schoenbaum EE, Hartel D, Lo Y, Howard AA, Floris-Moore M, Arnsten JH, et al. HIV infection, drug use, and onset of natural menopause. *Clin Infect Dis*. 2005 Nov 15;41(10):1517–24.
10. Santoro N. Perimenopause: From Research to Practice. *J Womens Health (Larchmt)*. 2016 Apr;25(4):332–9.
11. Chirwa M, Ma R, Guallar C, Tariq S. Managing menopause in women living with HIV: A survey of primary care practitioners. *Post Reprod Health*. 2017 Sep;23(3):111–5.
12. Zungu NP, Mabaso ML, Kumalo F, Sigida S, Mlangeni L, Wabiri N, et al. Prevalence of non-communicable diseases (NCDs) and associated factors among HIV positive educators: Findings from the 2015/6 survey of Health of Educators in Public Schools in South Africa. *PLoS One*. 2019 Feb 8;14(2):e0209756.
13. Friderichs T, Hall D. Postmenopausal symptoms in a group of rural Xhosa women. *South African Family Practice*. 2005 Jun 15;47(5):56–8.
14. Agaba P, Meloni S, Sule H, Ocheke A, Agaba E, Idoko J, et al. Factors associated with early menopause among women in Nigeria. 2017.
15. Yisma E, Eshetu N, Ly S, Dessalegn B. Prevalence and severity of menopause symptoms among perimenopausal and postmenopausal women aged 30-49 years in Gulele sub-city of Addis Ababa, Ethiopia. *BMC Womens Health*. 2017 Dec 8;17(1):124.
16. Fan MD, Maslow BS, Santoro N, Schoenbaum E. HIV and the menopause. *Menopause Int*. 2008 Dec 1;14(4):163–8.
17. Kruger T, Botha M. Menopause. In: *Clinical Gynaecology*. Third. Cape Town, South Africa: Juta & Co. Ltd; 2007. p. 332–41.
18. de Pommerol M, Hessamfar M, Lawson-Ayayi S, Neau D, Geffard S, Farbos S, et al. Menopause and HIV infection: age at onset and associated factors, ANRS CO3 Aquitaine cohort. *Int J STD AIDS*. 2011 Feb 1;22(2):67–72.
19. Bruce D, Rymer J. Symptoms of the menopause. *Best Pract Res Clin Obstet Gynaecol*. 2009 Feb;23(1):25–32.
20. Okhai H, Sabin C, Haag K, Sherr L, Dhairyawan R, Shephard J, et al. The Prevalence and Patterns of Menopausal Symptoms in Women Living with HIV. *AIDS Behav*. 2022 Nov 1;26(11):3679–87.



21. Madanhire T, Hawley S, Dauya E, Bandason T, Rukuni R, Ferrand RA, et al. Menopausal symptoms by HIV status and association with health-related quality of life among women in Zimbabwe: a cross-sectional study. *BMC Womens Health*. 2023 Jun 29;23(1):343.
22. Okhai H, Dragomir L, Pool ER, Sabin CA, Miners A, Sherr L, et al. Association between health-related quality of life and menopausal status and symptoms in women living with HIV aged 45–60 years in England: An analysis of the PRIME study. *Women's Health*. 2022 Jan 13;18:174550652110687.
23. Ambikairajah A, Walsh E, Cherbuin N. A review of menopause nomenclature. *Reprod Health*. 2022 Jan 31;19(1):29.
24. Utian WH. The International Menopause menopause-related terminology definitions. *Climacteric*. 1999 Jan 3;2(4):284–6.
25. Jankowska K. Premature ovarian failure. *Prz Menopauzalny*. 2017 Jun;16(2):51–6.
26. Chirwa M, Taghinejadi N, Macaulay G, Mandalia S, Bellone C, Panay N, et al. Reflections on a specialist HIV menopause service: Experiences of managing menopause in women living with HIV. *HIV Med*. 2022 Apr 1;23(4):426–33.
27. Hachfeld A, Atkinson A, Stute P, Calmy A, Tarr PE, Darling K, et al. Women with HIV transitioning through menopause: Insights from the Swiss HIV Cohort Study (SHCS). *HIV Med*. 2022 Apr 1;23(4):417–25.
28. Andany N, Kennedy VL, Aden M, Loutfy M. Perspectives on menopause and women with HIV. Vol. 8, *International Journal of Women's Health*. Dove Medical Press Ltd; 2016. p. 1–22.
29. Gold EB, Crawford SL, Avis NE, Crandall CJ, Matthews KA, Waetjen LE, et al. Factors Related to Age at Natural Menopause: Longitudinal Analyses From SWAN. *Am J Epidemiol*. 2013 Jul 1;178(1):70–83.
30. Canelón SP, Boland MR. A Systematic Literature Review of Factors Affecting the Timing of Menarche: The Potential for Climate Change to Impact Women's Health. *Int J Environ Res Public Health*. 2020 Mar 5;17(5).
31. Chirwa M, Taghinejadi N, Macaulay G, Mandalia S, Bellone C, Panay N, et al. Reflections on a specialist HIV menopause service. *HIV Med*. 2022 Apr 6;23(4):426–33.
32. Schoenaker DAJM, Jackson CA, Rowlands J V, Mishra GD. Socioeconomic position, lifestyle factors and age at natural menopause: a systematic review and meta-analyses of studies across six continents. *Int J Epidemiol* [Internet]. 2014 Oct 1;43(5):1542–62. Available from: <https://doi.org/10.1093/ije/dyu094>
33. Andarini S, Sujarwoto S. Early menarche and premature natural menopause in Indonesia. *Ann Hum Biol*. 2018 Jul 4;45(5):419–27.
34. Soules MR, Sherman S, Parrott E, Rebar R, Santoro N, Utian W, et al. Executive summary: Stages of Reproductive Aging Workshop (STRAW). *Fertil Steril*. 2001 Nov;76(5):874–8.
35. Harlow SD, Crawford S, Dennerstein L, Burger HG, Mitchell ES, Sowers MF, et al. Recommendations from a multi-study evaluation of proposed criteria for staging reproductive aging. *Climacteric*. 2007 Apr;10(2):112–9.
36. Gold EB, Bromberger J, Crawford S, Samuels S, Greendale GA, Harlow SD, et al. Factors Associated with Age at Natural Menopause in a Multiethnic Sample of Midlife Women [Internet]. Vol. 153, *American Journal of Epidemiology*. 2001. Available from: <https://academic.oup.com/aje/article/153/9/865/124589>
37. Van Ommen CE, King EM, Murray MCM. Age at menopause in women living with HIV: a systematic review. Vol. 28, *Menopause*. Wolters Kluwer Health; 2021. p. 1428–36.
38. Mishra GD, Pandeya N, Dobson AJ, Chung HF, Anderson D, Kuh D, et al. Early menarche, nulliparity and the risk for premature and early natural menopause. *Hum Reprod*. 2017 Mar 1;32(3):679–86.
39. Chan S, Gomes A, Singh RS. Is menopause still evolving? Evidence from a longitudinal study of multiethnic populations and its relevance to women's health. *BMC Womens Health*. 2020 Apr 19;20(1):74.



40. Schoenaker DA, Jackson CA, Rowlands J V, Mishra GD. Socioeconomic position, lifestyle factors and age at natural menopause: a systematic review and meta-analyses of studies across six continents. *Int J Epidemiol*. 2014 Oct;43(5):1542–62.
41. Calvet GA, Grinsztejn BGJ, Quintana MDSB, Derrico M, Jalil EM, Cytryn A, et al. Predictors of early menopause in HIV-infected women: A prospective cohort study. *Am J Obstet Gynecol*. 2015 Jun 1;212(6):765.e1-765.e13.
42. Henderson KD, Bernstein L, Henderson B, Kolonel L, Pike MC. Predictors of the timing of natural menopause in the Multiethnic Cohort Study. *Am J Epidemiol*. 2008 Jun 1;167(11):1287–94.
43. Schoenaker DAJM, Jackson CA, Rowlands J V, Mishra GD. Socioeconomic position, lifestyle factors and age at natural menopause: a systematic review and meta-analyses of studies across six continents. *Int J Epidemiol*. 2014 Oct;43(5):1542–62.
44. InterLACE Study Team. Variations in reproductive events across life: a pooled analysis of data from 505 147 women across 10 countries. *Hum Reprod*. 2019 May 1;34(5):881–93.
45. Kwawukume EY, Ghosh TS, Wilson JB. Menopausal age of Ghanaian women. *Int J Gynaecol Obstet*. 1993 Feb;40(2):151–5.
46. Frere G. Mean age at menopause and menarche in South Africa. *S Afr J Med Sci*. 1971 Jul;36(1):21–4.
47. Walker ARP, Walker BF, Ncongwane J, Tshabalala EN. Age of menopause in black women in South Africa. Vol. 91, *British Journal of Obstetrics and Gynaecology*. 1984.
48. Otolorin EO, Adeyefa I, Osotimehin BO, Fatinikun T, Ojengbede O, Otubu JO, et al. Clinical, hormonal and biochemical features of menopausal women in Ibadan, Nigeria. *Afr J Med Med Sci*. 1989 Dec;18(4):251–5.
49. Sammel MD, Freeman EW, Liu Z, Lin H, Guo W. Factors that influence entry into stages of the menopausal transition. *Menopause*. 2009;16(6):1218–27.
50. Bromberger JT, Matthews KA, Kuller LH, Wing RR, Meilahn EN, Plantinga P. Prospective Study of the Determinants of Age at Menopause. *Am J Epidemiol*. 1997 Jan 15;145(2):124–33.
51. Wise LA, Krieger N, Zierler S, Harlow BL. Lifetime socioeconomic position in relation to onset of perimenopause. *J Epidemiol Community Health* (1978). 2002 Nov;56(11):851–60.
52. Harlow BL, Signorello LB. Factors associated with early menopause. *Maturitas*. 2000 Apr 28;35(1):3–9.
53. Jaff NG, Snyman T, Norris SA, Crowther NJ. Staging reproductive aging using Stages of Reproductive Aging Workshop + 10 in black urban African women in the Study of Women Entering and in Endocrine Transition. *Menopause*. 2014 Nov;21(11):1225–33.
54. Calvet GA, Grinsztejn BGJ, Quintana M de SB, Derrico M, Jalil EM, Cytryn A, et al. Predictors of early menopause in HIV-infected women: a prospective cohort study. *Am J Obstet Gynecol*. 2015 Jun;212(6):765.e1-765.e13.
55. Scherzer R, Greenblatt RM, Merhi ZO, Kassaye S, Lambert-Messerlian G, Maki PM, et al. Use of antimüllerian hormone to predict the menopausal transition in HIV-infected women. *Am J Obstet Gynecol*. 2017 Jan;216(1):46.e1-46.e11.
56. Schwenkhagen A. Hormonal changes in menopause and implications on sexual health. *J Sex Med*. 2007 Mar;4 Suppl 3:220–6.
57. Walmsley S, Clarke R, Lee T, Singer J, Cheung AM, Smaill F, et al. BEING: Bone Health in Aging Women with HIV: Impact of Switching Antiretroviral Therapy on Bone Mineral Density During the Perimenopausal Period. *AIDS Res Hum Retroviruses*. 2023 Apr 1;39(4):204–10.
58. Agaba PA, Meloni ST, Sule HM, Ocheke AN, Agaba EI, Idoko JA, et al. Prevalence and predictors of severe menopause symptoms among HIV-positive and -negative Nigerian women. *Int J STD AIDS*. 2017 Nov 14;28(13):1325–34.
59. Paramsothy P, Harlow SD, Nan B, Greendale GA, Santoro N, Crawford SL, et al. Duration of the menopausal transition is longer in women with young age at onset: The multiethnic Study of Women's Health Across the Nation. *Menopause*. 2017;24(2):142–9.



60. Suarez-García I, Alejos B, Pérez-Elías MJ, Iribarren JA, Hernando A, Ramírez M, et al. How do women living with HIV experience menopause? Menopausal symptoms, anxiety and depression according to reproductive age in a multicenter cohort. *BMC Womens Health*. 2021 Dec 28;21(1):223.
61. Duff PK, Money DM, Ogilvie GS, Ranville F, Kestler M, Braschel MC, et al. Severe menopausal symptoms associated with reduced adherence to antiretroviral therapy among perimenopausal and menopausal women living with HIV in Metro Vancouver. *Menopause*. 2018 May;25(5):531–7.
62. Looby SE. Symptoms of menopause or symptoms of HIV? Untangling the knot. *Menopause*. 2018 Jul;25(7):728–30.
63. Solomon D, Sabin CA, Burns F, Gilson R, Allan S, de Ruiter A, et al. The association between severe menopausal symptoms and engagement with HIV care and treatment in women living with HIV. *AIDS Care - Psychological and Socio-Medical Aspects of AIDS/HIV*. 2021;33(1):101–8.
64. Madanhire T, Hawley S, Dauya E, Bandason T, Rukuni R, Ferrand RA, et al. Menopausal symptoms by HIV status and association with health-related quality of life among women in Zimbabwe: a cross-sectional study. *BMC Womens Health*. 2023 Jun 29;23(1):343.
65. Madanhire T, Hawley S, Dauya E, Bandason T, Rukuni R, Ferrand RA, et al. Menopausal symptoms by HIV status and association with health-related quality of life among women in Zimbabwe: a cross-sectional study. *BMC Womens Health*. 2023 Jun 29;23(1):343.
66. McKinlay SM, Brambilla DJ, Posner JG. The normal menopause transition. *Maturitas*. 1992 Jan;14(2):103–15.
67. Williams RE, Levine KB, Kalilani L, Lewis J, Clark R V. Menopause-specific questionnaire assessment in US population-based study shows negative impact on health-related quality of life. *Maturitas*. 2009 Feb 20;62(2):153–9.
68. Woods NF, Mitchell ES. Symptom interference with work and relationships during the menopausal transition and early postmenopause: observations from the Seattle Midlife Women's Health Study. *Menopause*. 2011 Jun;18(6):654–61.
69. Miller SA, Santoro N, Lo Y, Howard AA, Arnsten JH, Floris-Moore M, et al. Menopause symptoms in HIV-infected and drug-using women. Vol. 12, *Menopause*. 2005. p. 348–56.
70. Lui-Filho JF, Valadares ALR, Gomes DC, Amaral E, Pinto-Neto AM, Costa-Paiva L. Menopausal symptoms and associated factors in HIV-positive women. *Maturitas*. 2013;76(2):172–8.
71. Maki PM, Rubin LH, Cohen M, Golub ET, Greenblatt RM, Young M, et al. Depressive symptoms are increased in the early perimenopausal stage in ethnically diverse human immunodeficiency virus-infected and human immunodeficiency virus-uninfected women. *Menopause*. 2012 Nov;19(11):1215–23.
72. Sievert LL, Morrison L, Brown DE, Reza AM. Vasomotor symptoms among Japanese-American and European-American women living in Hilo, Hawaii. *Menopause*. 2007 Mar;14(2):261–9.
73. Jung SJ, Shin A, Kang D. Menarche age, menopause age and other reproductive factors in association with post-menopausal onset depression: Results from Health Examinees Study (HEXA). *J Affect Disord*. 2015 Nov 15;187:127–35.
74. Delavar MA, Hajiahmadi M. Factors Affecting the Age in Normal Menopause and frequency of Menopausal Symptoms in Northern Iran. *Iran Red Crescent Med J*. 2011 Mar;13(3):192–8.
75. Whiteley J, DiBonaventura M daCosta, Wagner JS, Alvir J, Shah S. The Impact of Menopausal Symptoms on Quality of Life, Productivity, and Economic Outcomes. *J Womens Health*. 2013 Nov;22(11):983–90.
76. Ayers B, Hunter MS. Health-related quality of life of women with menopausal hot flashes and night sweats. *Climacteric*. 2013 Apr;16(2):235–9.
77. Conde DM, Pinto-Neto AM, Santos-Sá D, Costa-Paiva L, Martinez EZ. Factors associated with quality of life in a cohort of postmenopausal women. *Gynecol Endocrinol*. 2006 Aug;22(8):441–6.
78. El Shafie K, Al Farsi Y, Al Zadjali N, Al Adawi S, Al Busaidi Z, Al Shafae M. Menopausal symptoms among healthy, middle-aged Omani women as assessed with the Menopause Rating Scale. *Menopause*. 2011 Oct;18(10):1113–9.



79. Singh M. Early age of natural menopause in India, a biological marker for early preventive health programs. *Climacteric*. 2012 Dec;15(6):581–6.
80. Krajewska K, Krajewska-Kulak E, Heineman L, Adraniotis J, Chadzopulu A, Theodosopoyloy E, et al. Comparative analysis of quality of life women in menopause period in Poland, Greece and Belorussia using MRS Scale. Preliminary report. *Adv Med Sci*. 2007;52 Suppl 1:140–3.
81. Maki PM, Springer G, Anastos K, Gustafson DR, Weber K, Vance D, et al. Cognitive changes during the menopausal transition: a longitudinal study in women with and without HIV. *Menopause*. 2021 Apr 11;28(4):360–8.
82. Kodoth V, Scaccia S, Aggarwal B. Adverse Changes in Body Composition During the Menopausal Transition and Relation to Cardiovascular Risk: A Contemporary Review. *Women's Health Reports*. 2022 Jun 1;3(1):573–81.
83. Li C, Borgfeldt C, Samsioe G, Lidfeldt J, Nerbrand C. Background factors influencing somatic and psychological symptoms in middle-age women with different hormonal status. *Maturitas*. 2005 Nov;52(3–4):306–18.
84. Ashraf AN, Okhai H, Sabin CA, Sherr L, Haag K, Dhairyawan R, et al. Obesity in women living with HIV aged 45–60 in England: An analysis of the PRIME study. *HIV Med*. 2022 Apr 18;23(4):371–7.
85. Jaff NG, Norris SA, Snyman T, Toman M, Crowther NJ. Body composition in the Study of Women Entering and in Endocrine Transition (SWEET): A perspective of African women who have a high prevalence of obesity and HIV infection. *Metabolism*. 2015 Sep;64(9):1031–41.
86. Bares SH, Smeaton LM, Xu A, Godfrey C, McComsey GA. HIV-Infected Women Gain More Weight than HIV-Infected Men Following the Initiation of Antiretroviral Therapy. *J Womens Health*. 2018 Sep;27(9):1162–9.
87. Gradidge PJL, Crowther NJ. Review: Metabolic Syndrome in Black South African Women. *Ethn Dis*. 2017;27(2):189–200.
88. Savinelli S, De Francesco D, Feeney ER, Babalis D, Bagkeris E, Post FA, et al. Factors associated with obesity in the Pharmacokinetic and Clinical Observations in People over Fifty (POPPY) cohort: an observational cross-sectional analysis. *HIV Med*. 2020 Aug;21(7):441–52.
89. Ilozue C, Howe B, Shaw S, Haigh K, Hussey J, Price DA, et al. Obesity in the HIV-infected population in Northeast England: a particular issue in Black-African women. *Int J STD AIDS*. 2017 Mar;28(3):284–9.
90. Boodram B, Plankey MW, Cox C, Tien PC, Cohen MH, Anastos K, et al. Prevalence and correlates of elevated body mass index among HIV-positive and HIV-negative women in the Women's Interagency HIV Study. *AIDS Patient Care STDS*. 2009 Dec;23(12):1009–16.
91. Cortés YI, Yin MT, Reame NK. Bone Density and Fractures in HIV-infected Postmenopausal Women: A Systematic Review. *Journal of the Association of Nurses in AIDS Care*. 2015 Jul 1;26(4):387–98.
92. Riggs BL, Khosla S, Melton LJ. Sex steroids and the construction and conservation of the adult skeleton. *Endocr Rev*. 2002 Jun;23(3):279–302.
93. Sowers M, Zheng H, Tomey K, Karvonen-Gutierrez C, Jannausch M, Li X, et al. Changes in body composition in women over six years at midlife: ovarian and chronological aging. *J Clin Endocrinol Metab*. 2007 Mar;92(3):895–901.
94. Khosla S, Melton LJ, Riggs BL. The unitary model for estrogen deficiency and the pathogenesis of osteoporosis: is a revision needed? *J Bone Miner Res*. 2011 Mar;26(3):441–51.
95. Finnerty F, Walker-Bone K, Tariq S. Osteoporosis in postmenopausal women living with HIV. *Maturitas*. 2017 Jan;95:50–4.
96. Looby SED. Menopause-associated metabolic manifestations and symptomatology in HIV infection: a brief review with research implications. *J Assoc Nurses AIDS Care*. 2012;23(3):195–203.
97. Slemenda CW, Longcope C, Zhou L, Hui SL, Peacock M, Johnston CC. Sex steroids and bone mass in older men. Positive associations with serum estrogens and negative associations with androgens. *J Clin Invest*. 1997 Oct 1;100(7):1755–9.



98. Cummings SR, San Martin J, McClung MR, Siris ES, Eastell R, Reid IR, et al. Denosumab for prevention of fractures in postmenopausal women with osteoporosis. *N Engl J Med*. 2009 Aug 20;361(8):756–65.
99. Riggs BL, Melton LJ. Involutional osteoporosis. *N Engl J Med*. 1986 Jun 26;314(26):1676–86.
100. Compston J. Type 2 diabetes mellitus and bone. *J Intern Med*. 2018 Feb;283(2):140–53.
101. Compston J. HIV infection and osteoporosis. *Bonekey Rep*. 2015 Feb 11;4.
102. Dolan SE, Huang JS, Killilea KM, Sullivan MP, Aliabadi N, Grinspoon S. Reduced bone density in HIV-infected women. *AIDS*. 2004 Feb;18(3):475–83.
103. Yin MT, Zhang CA, McMahon DJ, Ferris DC, Irani D, Colon I, et al. Higher rates of bone loss in postmenopausal HIV-infected women: a longitudinal study. *J Clin Endocrinol Metab*. 2012 Feb;97(2):554–62.
104. Yin MT, Shiao S, Rimland D, Gibert CL, Bedimo RJ, Rodriguez-Barradas MC, et al. Fracture Prediction With Modified-FRAX in Older HIV-Infected and Uninfected Men. *J Acquir Immune Defic Syndr*. 2016 Aug 15;72(5):513–20.
105. McComsey GA, Tebas P, Shane E, Yin MT, Overton ET, Huang JS, et al. Bone disease in HIV infection: a practical review and recommendations for HIV care providers. *Clin Infect Dis*. 2010 Oct 15;51(8):937–46.
106. Thomas J, Doherty SM. HIV infection--a risk factor for osteoporosis. *J Acquir Immune Defic Syndr*. 2003 Jul 1;33(3):281–91.
107. Biver E. Osteoporosis and HIV Infection. *Calcif Tissue Int*. 2022 May;110(5):624–40.
108. Rothman MS, Bessesen MT. HIV infection and osteoporosis: pathophysiology, diagnosis, and treatment options. *Curr Osteoporos Rep*. 2012 Dec;10(4):270–7.
109. Brown TT, Qaqish RB. Antiretroviral therapy and the prevalence of osteopenia and osteoporosis: a meta-analytic review. *AIDS*. 2006 Nov 14;20(17):2165–74.
110. Güerri-Fernandez R, Vestergaard P, Carbonell C, Knobel H, Avilés FF, Castro AS, et al. HIV infection is strongly associated with hip fracture risk, independently of age, gender, and comorbidities: a population-based cohort study. *J Bone Miner Res*. 2013 Jun;28(6):1259–63.
111. Compston J. Osteoporosis and fracture risk associated with HIV infection and treatment. *Endocrinol Metab Clin North Am*. 2014 Sep;43(3):769–80.
112. Battalora LA, Young B, Overton ET. Bones, Fractures, Antiretroviral Therapy and HIV. *Curr Infect Dis Rep*. 2014 Feb;16(2):393.
113. Shiao S, Broun EC, Arpad SM, Yin MT. Incident fractures in HIV-infected individuals: a systematic review and meta-analysis. *AIDS*. 2013 Jul 31;27(12):1949–57.
114. Prieto-Alhambra D, Güerri-Fernández R, De Vries F, Lalmohamed A, Bazelier M, Starup-Linde J, et al. HIV infection and its association with an excess risk of clinical fractures: a nationwide case-control study. *J Acquir Immune Defic Syndr*. 2014 May 1;66(1):90–5.
115. Ahmed M, Mital D, Abubaker NE, Panourgia M, Owles H, Papadaki I, et al. Bone Health in People Living with HIV/AIDS: An Update of Where We Are and Potential Future Strategies. *Microorganisms*. 2023 Mar 19;11(3).
116. Amorosa V, Tebas P. Bone disease and HIV infection. *Clin Infect Dis*. 2006 Jan 1;42(1):108–14.
117. Tebas P, Powderly WG, Claxton S, Marin D, Tantisiriwat W, Teitelbaum SL, et al. Accelerated bone mineral loss in HIV-infected patients receiving potent antiretroviral therapy. *AIDS*. 2000 Mar 10;14(4):F63–7.
118. McComsey GA, Kitch D, Daar ES, Tierney C, Jahed NC, Tebas P, et al. Bone Mineral Density and Fractures in Antiretroviral-Naïve Persons Randomized to Receive Abacavir-Lamivudine or Tenofovir Disoproxil Fumarate-Emtricitabine Along With Efavirenz or Atazanavir-Ritonavir: AIDS Clinical Trials Group A5224s, a Substudy of ACTG A5202. *J Infect Dis*. 2011 Jun 15;203(12):1791–801.



119. Alonge TO, Okoje-Adesomoju VN, Atalabi OM, Obamuyide HA, Olaleye D, Adewole IF. Prevalence of abnormal bone mineral density in hiv-positive patients in ibadan, Nigeria. *J West Afr Coll Surg*. 2013;3(4):1–14.
120. Triant VA, Brown TT, Lee H, Grinspoon SK. Fracture prevalence among human immunodeficiency virus (HIV)-infected versus non-HIV-infected patients in a large U.S. healthcare system. *J Clin Endocrinol Metab*. 2008 Sep;93(9):3499–504.
121. Matovu FK, Pettifor JM, Compston JE. HIV and Bone Health: Considerations for Menopausal Women Living with HIV in Sub-Saharan Africa. *Journal of Bone and Mineral Research*. 2020 Dec 1;38(5):617–8.
122. Compston J. HIV infection and bone disease. *J Intern Med*. 2016 Oct 6;280(4):350–8.
123. Biver E. Osteoporosis and HIV Infection. *Calcif Tissue Int*. 2022 May;110(5):624–40.
124. Kruger MJ, Nell TA. Bone mineral density in people living with HIV: a narrative review of the literature. *AIDS Res Ther*. 2017 Dec 26;14(1):35.
125. Gregson CL, Madanhire T, Rehman A, Ferrand RA, Cappola AR, Tollman S, et al. Osteoporosis, Rather Than Sarcopenia, Is the Predominant Musculoskeletal Disease in a Rural South African Community Where Human Immunodeficiency Virus Prevalence Is High: A Cross-Sectional Study. *J Bone Miner Res*. 2022 Feb;37(2):244–55.
126. Ó Breasail M, Pearse C, Zengin A, Jarjou L, Cooper C, Ebeling PR, et al. Longitudinal Change in Bone Density, Geometry, and Estimated Bone Strength in Older Men and Women From The Gambia: Findings From the Gambian Bone and Muscle Aging Study (GambAS). *J Bone Miner Res*. 2023 Jan;38(1):48–58.
127. Matovu FK, Pettifor JM, Compston JE. HIV and Bone Health: Considerations for Menopausal Women Living with HIV in Sub-Saharan Africa. *Journal of Bone and Mineral Research*. 2020 Dec 1;38(5):617–8.
128. Matovu FK, Wattanachanya L, Beksinska M, Pettifor JM, Ruxrungtham K. Bone health and HIV in resource-limited settings: a scoping review. *Curr Opin HIV AIDS*. 2016 May;11(3):306–25.
129. Sharma A, Flom PL, Rosen CJ, Schoenbaum EE. Racial differences in bone loss and relation to menopause among HIV-infected and uninfected women. *Bone*. 2015 Aug;77:24–30.
130. Jespersen NA, Axelsen F, Dollerup J, Nørgaard M, Larsen CS. The burden of non-communicable diseases and mortality in people living with HIV (PLHIV) in the pre-, early- and late-HAART era. *HIV Med*. 2021 Jul;22(6):478–90.
131. Goh SSL, Lai PSM, Tan ATB, Ponnampalavanar S. Reduced bone mineral density in human immunodeficiency virus-infected individuals: a meta-analysis of its prevalence and risk factors: supplementary presentation. *Osteoporos Int*. 2018 Jul;29(7):1683.
132. Gregson CL, Madanhire T, Rehman A, Ferrand RA, Cappola AR, Tollman S, et al. Osteoporosis, Rather Than Sarcopenia, Is the Predominant Musculoskeletal Disease in a Rural South African Community Where Human Immunodeficiency Virus Prevalence Is High: A Cross-Sectional Study. *J Bone Miner Res*. 2022 Feb;37(2):244–55.
133. Sharma A, Hoover DR, Shi Q, Tien PC, Weber KM, Shah JG, et al. Human Immunodeficiency Virus (HIV) and Menopause Are Independently Associated With Lower Bone Mineral Density: Results From the Women's Interagency HIV Study. *Clinical Infectious Diseases*. 2022 Aug 24;75(1):65–72.
134. Matovu FK, Pettifor JM, Compston JE. HIV and Bone Health: Considerations for Menopausal Women Living with HIV in Sub-Saharan Africa. *Journal of Bone and Mineral Research*. 2020 Dec 1;38(5):617–8.
135. Moran CA, Weitzmann MN, Ofotokun I. Bone Loss in HIV Infection. *Curr Treat Options Infect Dis*. 2017 Mar;9(1):52–67.
136. Dolan SE, Huang JS, Killilea KM, Sullivan MP, Aliabadi N, Grinspoon S. Reduced bone density in HIV-infected women. *AIDS*. 2004 Feb 20;18(3):475–83.



137. Bonjoch A, Figueras M, Estany C, Perez-Alvarez N, Rosales J, del Rio L, et al. High prevalence of and progression to low bone mineral density in HIV-infected patients: a longitudinal cohort study. *AIDS*. 2010 Nov 27;24(18):2827–33.
138. Ó Breasail M, Gregson CL, Norris SA, Madanhire T, Jaff N, Crowther NJ, et al. Menopause is associated with bone loss, particularly at the distal radius, in black South African women: Findings from the Study of Women Entering and in Endocrine Transition (SWEET). *Bone*. 2022 Nov;164:116543.
139. Madanhire T, Goedecke JH, Ward KA, Jaff N, Crowther NJ, Norris S, et al. The Impact of Human Immunodeficiency Virus and Menopause on Bone Mineral Density: A Longitudinal Study of Urban-Dwelling South African Women. *Journal of Bone and Mineral Research*. 2023 May 1;38(5):619–30.
140. Stone L, Looby SE, Zanni M V. Cardiovascular disease risk among women living with HIV in North America and Europe. *Curr Opin HIV AIDS*. 2017 Nov;12(6):585–93.
141. Womack JA, Chang CH, So-Armah KA, Alcorn C, Baker J V., Brown ST, et al. HIV Infection and Cardiovascular Disease in Women. *J Am Heart Assoc*. 2014 Sep 16;3(5).
142. Solomon D, Sabin CA, Mallon PWG, Winston A, Tariq S. Cardiovascular disease in women living with HIV: A narrative review. Vol. 108, *Maturitas*. Elsevier Ireland Ltd; 2018. p. 58–70.
143. Dolan SE, Hadigan C, Killilea KM, Sullivan MP, Hemphill L, Lees RS, et al. Increased Cardiovascular Disease Risk Indices in HIV-Infected Women [Internet]. Available from: <http://journals.lww.com/jaids>
144. Cortés YI, Reame N, Zeana C, Jia H, Ferris DC, Shane E, et al. Cardiovascular Risk in HIV-Infected and Uninfected Postmenopausal Minority Women: Use of the Framingham Risk Score. *J Womens Health*. 2017 Mar 1;26(3):241–8.
145. Nagata C, Takatsuka N, Inaba S, Kawakami N, Shimizu H. Association of diet and other lifestyle with onset of menopause in Japanese women. *Maturitas*. 1998 Jun 3;29(2):105–13.
146. Sherman BM, Wallace RB, Bean JA, Chang Y, Schlabaugh L. The relationship of menopausal hot flushes to medical and reproductive experience. *J Gerontol*. 1981 May;36(3):306–9.
147. Willett W, Stampfer MJ, Bain C, Lipnick R, Speizer FE, Rosner B, et al. Cigarette smoking, relative weight, and menopause. *Am J Epidemiol*. 1983 Jun;117(6):651–8.
148. Sharma A, Flom PL, Weedon J, Klein RS. Prospective study of bone mineral density changes in aging men with or at risk for HIV infection. *AIDS*. 2010 Sep 24;24(15):2337–45.
149. Looby SE, Shifren J, Corless I, Rope A, Pedersen MC, Joffe H, et al. Increased hot flash severity and related interference in perimenopausal human immunodeficiency virus-infected women. *Menopause*. 2014 Apr;21(4):403–9.
150. Boonyanurak P, Bunupuradah T, Wilawan K, Lueanyod A, Thongpaeng P, Chatvong D, et al. Age at menopause and menopause-related symptoms in human immunodeficiency virus–infected Thai women. *Menopause*. 2012 Jul;19(7):820–4.
151. Ferreira CE, Pinto-Neto AM, Conde DM, Costa-Paiva L, Morais SS, Magalhães J. Menopause symptoms in women infected with HIV: Prevalence and associated factors. *Gynecological Endocrinology*. 2007 Jan 7;23(4):198–205.
152. Raffe S, Sabin C, Gilleece Y, Women Against Viruses in Europe (WAVE) EACS. Comorbidities in women living with HIV: A systematic review. *HIV Med*. 2022 Apr;23(4):331–61.
153. Rivas P, Górgolas M, García-Delgado R, Díaz-Curiel M, Goyenechea A, Fernández-Guerrero ML. Evolution of bone mineral density in AIDS patients on treatment with zidovudine/lamivudine plus abacavir or lopinavir/ritonavir. *HIV Med*. 2008 Feb;9(2):89–95.
154. Cazanave C, Dupon M, Lavignolle-Aurillac V, Barthe N, Lawson-Ayayi S, Mehse N, et al. Reduced bone mineral density in HIV-infected patients: prevalence and associated factors. *AIDS*. 2008 Jan 30;22(3):395–402.
155. Stellbrink H, Orkin C, Arribas JR, Compston J, Gerstoft J, Van Wijngaerden E, et al. Comparison of Changes in Bone Density and Turnover with Abacavir-Lamivudine versus Tenofovir-Emtricitabine in HIV-Infected Adults: 48-Week Results from the ASSERT Study. *Clinical Infectious Diseases*. 2010 Oct 15;51(8):963–72.



156. Teichmann J, Stephan E, Lange U, Discher T, Friese G, Lohmeyer J, et al. Osteopenia in HIV-infected women prior to highly active antiretroviral therapy. *J Infect.* 2003 May;46(4):221–7.
157. Brown TT, Ross AC, Storer N, Labbato D, McComsey GA. Bone Turnover, Osteoprotegerin/Rankl and Inflammation with Antiretroviral Initiation: Tenofovir versus Non-Tenofovir Regimens. *Antivir Ther.* 2011 Oct 1;16(7):1063–72.
158. Shema Tariq, Richard Gilson, Fiona Burns, Andrew Copas, Caroline Sabin. Positive tRansltions through Menopause (PRIME) [Internet]. England; 2018 [cited 2024 Jun 17]. Available from: <https://www.ucl.ac.uk/global-health/research/a-z/PRIME>
159. Chirwa M, Ma R, Guallar C, Tariq S. Managing menopause in women living with HIV: A survey of primary care practitioners. *Post Reprod Health.* 2017 Sep 1;23(3):111–5.
160. Loutfy MR, Sherr L, Sonnenberg-Schwan U, Walmsley SL, Johnson M, d'Arminio Monforte A. Caring for women living with HIV: gaps in the evidence. *J Int AIDS Soc.* 2013 Jan;16(1).
161. Agaba P, Meloni S, Sule H, Ocheke A, Agaba E, Idoko J, et al. Factors associated with early menopause among women in Nigeria [Internet]. 2017 [cited 2023 Oct 19]. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5518243/>
162. Adam GP, Di M, Cu-Uvin S, Halladay C, Smith BT, Iyer S, et al. Strategies for improving the lives of US women aged 40 and above living with HIV/AIDS: an evidence map. *Syst Rev.* 2018 Feb 2;7(1):25.
163. Imai K, Sutton MY, Mdodo R, del Rio C. HIV and Menopause: A Systematic Review of the Effects of HIV Infection on Age at Menopause and the Effects of Menopause on Response to Antiretroviral Therapy. *Obstet Gynecol Int.* 2013;2013:1–11.
164. Palefsky J. Human papillomavirus-related disease in people with HIV. *Curr Opin HIV AIDS.* 2009 Jan;4(1):52–6.
165. Heinemann K, Ruebig A, Potthoff P, Schneider HPG, Strelow F, Heinemann LAJ, et al. The Menopause Rating Scale (MRS) scale: a methodological review. *Health Qual Life Outcomes.* 2004 Sep 2;2:45.
166. Graham EE, Michala L, Hachfeld A, Moseholm E. Collection of menopause data in studies of women living with : A systematic literature review. *HIV Med.* 2024 Feb 30;25(2):174–87.
167. Harlow SD, Gass M, Hall JE, Lobo R, Maki P, Rebar RW, et al. Executive summary of the Stages of Reproductive Aging Workshop + 10: addressing the unfinished agenda of staging reproductive aging. *Menopause.* 2012 Apr;19(4):387–95.
168. Soules MR, Sherman S, Parrott E, Rebar R, Santoro N, Utian W, et al. Stages of Reproductive Aging Workshop (STRAW). *J Womens Health Gend Based Med.* 2001 Nov;10(9):843–8.
169. Harlow SD, Mitchell ES, Crawford S, Nan B, Little R, Taffe J, et al. The ReSTAGE Collaboration: defining optimal bleeding criteria for onset of early menopausal transition. *Fertil Steril.* 2008 Jan;89(1):129–40.
170. van Rooij IAJ, Broekmans FJM, te Velde ER, Fauser BCJM, Bancsi LFJMM, de Jong FH, et al. Serum anti-Müllerian hormone levels: a novel measure of ovarian reserve. *Hum Reprod.* 2002 Dec;17(12):3065–71.
171. Kevenaar ME, Meerasahib MF, Kramer P, van de Lang-Born BMN, de Jong FH, Groome NP, et al. Serum anti-mullerian hormone levels reflect the size of the primordial follicle pool in mice. *Endocrinology.* 2006 Jul;147(7):3228–34.
172. Feyereisen E, Méndez Lozano DH, Taieb J, Hesters L, Frydman R, Fanchin R. Anti-Müllerian hormone: clinical insights into a promising biomarker of ovarian follicular status. *Reprod Biomed Online.* 2006 Jun;12(6):695–703.
173. de Vet A, Laven JSE, de Jong FH, Themmen APN, Fauser BCJM. Antimüllerian hormone serum levels: a putative marker for ovarian aging. *Fertil Steril.* 2002 Feb;77(2):357–62.
174. Howells P, Modarres M, Samuel M, Taylor C, Hamoda H. Experience of hormone replacement therapy in postmenopausal women living with HIV. *Post Reprod Health.* 2019 Jun;25(2):80–5.



175. Duff PK, Money DM, Ogilvie GS, Ranville F, Kestler M, Braschel MC, et al. Severe menopausal symptoms associated with reduced adherence to antiretroviral therapy among perimenopausal and menopausal women living with HIV in Metro Vancouver. *Menopause*. 2018 May;25(5):531–7.
176. Caixas U, Tariq S, Morello J, Dragovic G, Lourida G, Hachfeld A, et al. Comorbidities and menopause assessment in women living with HIV: a survey of healthcare providers across the WHO European region. *AIDS Care*. 2024 Jan 2;36(1):107–14.
177. Kojic EM, Wang CC, Cu-Uvin S. HIV and menopause: A review. Vol. 16, *Journal of Women's Health*. 2007. p. 1402–11.
178. Vigneswaran K, Hamoda H. Hormone replacement therapy - Current recommendations. *Best Pract Res Clin Obstet Gynaecol*. 2022 May;81:8–21.
179. Bowser DM, Utz S, Glick D, Harmon R. A Systematic Review of the Relationship of Diabetes Mellitus, Depression, and Missed Appointments in a Low-Income Uninsured Population. *Arch Psychiatr Nurs*. 2010 Oct;24(5):317–29.
180. Tariq S, Anderson J, Burns F, Delpech V, Gilson R, Sabin C. The menopause transition in women living with HIV: current evidence and future avenues of research. *J Virus Erad*. 2016 Apr 1;2(2):114–6.
181. King EM, Prior JC, Pick N, van Schalkwyk J, Kestler M, Tkachuk S, et al. Menopausal hormone therapy for women living with HIV. Vol. 8, *The Lancet HIV*. Elsevier Ltd; 2021. p. e591–8.
182. Andany N, Kaida A, de Pokomandy A, Yudin MH, Wang L, Kennedy VL, et al. Prevalence and correlates of early-onset menopause among women living with HIV in Canada. *Menopause*. 2020 Jan;27(1):66–75.
183. Yasui T, Hayashi K, Mizunuma H, Kubota T, Aso T, Matsumura Y, et al. Factors associated with premature ovarian failure, early menopause and earlier onset of menopause in Japanese women. *Maturitas*. 2012 Jul;72(3):249–55.
184. Johnson TM, Cohen HW, Howard AA, Santoro N, Floris-Moore M, Arnsten JH, et al. Attribution of menopause symptoms in human immunodeficiency virus-infected or at-risk drug-using women. *Menopause*. 2008 May;15(3):551–7.
185. Avis NE, Crawford SL, Greendale G, Bromberger JT, Everson-Rose SA, Gold EB, et al. Duration of menopausal vasomotor symptoms over the menopause transition. *JAMA Intern Med*. 2015 Apr;175(4):531–9.
186. Arnsten JH, Freeman R, Howard AA, Floris-Moore M, Santoro N, Schoenbaum EE. HIV Infection and Bone Mineral Density in Middle-Aged Women. *Clinical Infectious Diseases*. 2006 Apr 1;42(7):1014–20.
187. Yin M, Dobkin J, Brudney K, Becker C, Zadel JL, Manandhar M, et al. Bone mass and mineral metabolism in HIV+ postmenopausal women. *Osteoporosis International*. 2005 Nov;16(11):1345–52.
188. Finkelstein JS, Brockwell SE, Mehta V, Greendale GA, Sowers MR, Ettinger B, et al. Bone Mineral Density Changes during the Menopause Transition in a Multiethnic Cohort of Women. *J Clin Endocrinol Metab*. 2008 Mar 1;93(3):861–8.
189. May MT, Gompels M, Delpech V, Porter K, Orkin C, Kegg S, et al. Impact on life expectancy of HIV-1 positive individuals of CD4+ cell count and viral load response to antiretroviral therapy. *AIDS*. 2014 May 15;28(8):1193–202.
190. Maulide Cane R, Melesse DY, Kayeyi N, Manu A, Wado YD, Barros A, et al. HIV trends and disparities by gender and urban–rural residence among adolescents in sub-Saharan Africa. *Reprod Health*. 2021 Jun 17;18(S1):120.
191. Ellis C, Kruger HS, Viljoen M, Dave JA, Kruger MC. Factors associated with bone mineral density and bone resorption markers in postmenopausal hiv-infected women on antiretroviral therapy: A prospective cohort study. *Nutrients*. 2021 Jun 1;13(6).
192. Ramjee G, Daniels B. Women and HIV in Sub-Saharan Africa. *AIDS Res Ther*. 2013;10(1):30.
193. Ramjee G, Daniels B. Women and HIV in Sub-Saharan Africa [Internet]. 2013. Available from: <http://www.aidsrestherapy.com/content/10/1/30>

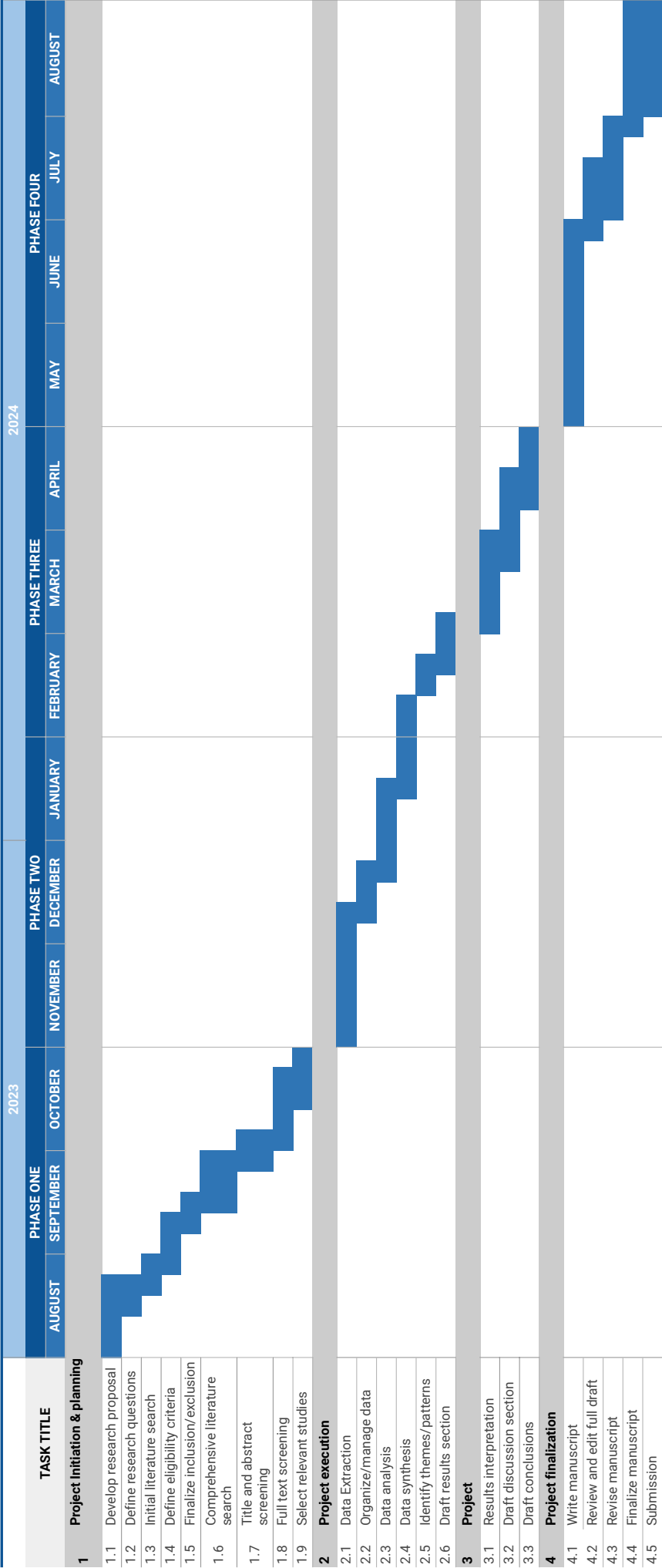


194. Dragovic B, Rymer J, Nwokolo N. Menopause care in women living with HIV in the UK - A review. *J Virus Erad.* 2022 Mar;8(1):100064.
195. Andany N, Kennedy VL, Aden M, Loutfy M. Perspectives on menopause and women with HIV. *Int J Womens Health.* 2016;8:1–22.
196. Munn Z, Peters MDJ, Stern C, Tufanaru C, McArthur A, Aromataris E. Systematic review or scoping review? Guidance for authors when choosing between a systematic or scoping review approach. *BMC Med Res Methodol.* 2018 Nov 19;18(1):143.
197. Levac D, Colquhoun H, O'Brien KK. Scoping studies: advancing the methodology. *Implement Sci.* 2010 Sep 20;5:69.
198. Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, et al. PRISMA Extension for Scoping Reviews (PRISMA-ScR): Checklist and Explanation. *Ann Intern Med.* 2018 Oct 2;169(7):467–73.
199. Arksey H, O'Malley L. Scoping studies: towards a methodological framework. *Int J Soc Res Methodol.* 2005 Feb;8(1):19–32.
200. Peters MDJ, Godfrey CM, Khalil H, McInerney P, Parker D, Soares CB. Guidance for conducting systematic scoping reviews. *Int J Evid Based Healthc.* 2015 Sep;13(3):141–6.
201. Peters MDJ, Marnie C, Tricco AC, Pollock D, Munn Z, Alexander L, et al. Updated methodological guidance for the conduct of scoping reviews. *JBIM Evid Synth.* 2020 Oct;18(10):2119–26.
202. Khalil H, Peters M, Godfrey CM, McInerney P, Soares CB, Parker D. An Evidence-Based Approach to Scoping Reviews. *Worldviews Evid Based Nurs.* 2016 Apr;13(2):118–23.
203. Mak S, Thomas A. Steps for Conducting a Scoping Review. *J Grad Med Educ.* 2022 Oct;14(5):565–7.
204. Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, et al. PRISMA Extension for Scoping Reviews (PRISMA-ScR): Checklist and Explanation. *Ann Intern Med.* 2018 Oct 2;169(7):467–73.
205. Manietta C, Quasdorf T, Rommerskirch-Manietta M, Braunwarth JI, Purwins D, Roes M. Protocol for conducting scoping reviews to map implementation strategies in different care settings: focusing on evidence-based interventions for preselected phenomena in people with dementia. *BMJ Open.* 2021 Sep 7;11(9):e051611.
206. Pollock D, Tricco AC, Peters MDJ, McInerney PA, Khalil H, Godfrey CM, et al. Methodological quality, guidance, and tools in scoping reviews: a scoping review protocol. *JBIM Evid Synth.* 2022 Apr 1;20(4):1098–105.
207. Peters MDJ, Godfrey CM, Khalil H, McInerney P, Parker D, Soares CB. Guidance for conducting systematic scoping reviews. *Int J Evid Based Healthc.* 2015 Sep;13(3):141–6.
208. Covidence [Internet]. 2024 [cited 2024 Jun 26]. Available from: <https://www.covidence.org/>
209. Mendeley [Internet]. 2024 [cited 2024 Jun 26]. Available from: <https://www.mendeley.com/>



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RESEARCH PROTOCOL



Appendix II

Table 4: Search strategy for each database

Database:	Search Terms:
PubMed	((((((((("Women with HIV") OR (((((((((Women) OR (WLHIV)) OR ("HIV-positive women")) OR ("Women living with HIV")) OR (HIV-Infected Women)) OR (Women*)) OR ("HIV-1-Infected Women")) OR ("human immunodeficiency virus-infected women")) OR ("women"[MeSH Terms])))) OR (WWH)) OR ("Ageing women")) OR ("Midlife women")) OR ("Women aged 40 and above")) AND (((((((((HIV) OR (AIDS)) OR (HIV*)) OR (AIDS*)) OR ("Human Immunodeficiency Virus")) OR ("acquired immunodeficiency syndrome"[MeSH Terms])) OR ("hiv"[MeSH Terms])) OR ("acquired immunodeficiency syndrome") OR ("HIV-1")) OR ("HIV 1")))) AND (((((((((((((((Menopause*) OR (Menopause)) OR (Postmenopausal)) OR (Perimenopausal)) OR (Menopause)) OR (((((Menopause*) OR (Menopause)) OR (Postmenopausal)) OR (Perimenopausal)) OR (Menopause))) OR ("Menopause"[Mesh])) OR (menopausal)) OR (postmenopause)) OR (perimenopause)) OR (menopaus*)) OR ("pre-menopaus*")) OR ("post menopaus*")) OR ("pre menopaus*")) OR ("post menopaus*")))) AND (((((((((Africa) OR (Africa*)) OR ("Sub-Saharan Africa")) OR (Africa [MeSH])) OR (Africa South of the Sahara [MeSH])) OR (Subsaharan Africa)) OR (subsaharan)) OR ("South Africa"))
Science Direct	(Menopause OR Menopausal OR perimenopausal OR postmenopausal) AND (HIV AND (Africa OR "Sub-Saharan Africa"))
Google Scholar	(Menopause OR Menopausal OR perimenopausal OR postmenopausal) AND (HIV AND (Africa OR "Sub-Saharan Africa"))

Appendix III

Table 5: Search keywords according to the JBI PCC concept

PCC elements	Criteria	Search keywords
P (Patient/Population)	Women living with HIV	Women OR WLHIV OR "Women living with HIV" OR "Women with HIV" OR WWH OR HIV-Infected Women OR "Older women living with HIV" OR OWLH OR HIV-positive women OR ageing OR "Women aged 40 and above" OR HIV OR Human Immunodeficiency Virus OR Human immunodeficiency virus-infected Women
C (Concept)	Menopause	Hormone Therapy OR HRT OR Hormone Replacement Therapy OR Menopause Therapy OR Menopause OR Perimenopausal OR Postmenopausal OR Menopausal OR Menopausal hormone therapy OR MHT OR menopaus*, pre-menopaus*, post-menopaus*, "pre menopaus*" and "post menopaus"
C (Context)	Sub-Saharan Africa	Africa* OR Sub-Saharan Africa OR Subsaharan Africa OR South Africa Angola OR Benin OR Botswana OR "Burkina Faso" OR Burundi OR "Cabo Verde" OR Cameroon OR Cameroun OR "Canary Islands" OR "Cape Verde" OR "Central Africa" OR "Central African Republic" OR Chad OR Comoros OR Congo OR "Cote d'Ivoire" OR "Democratic Republic of Congo" OR Djibouti OR "Eastern Africa" OR Eritrea OR eSwatini OR Ethiopia OR Gabon OR Gambia OR Ghana OR Guinea OR Guinea-Bissau OR "Ivory Coast" OR Jamahiriya OR Kenya OR Lesotho OR Liberia OR Madagascar OR Malawi OR Mali OR Mauritania OR Mauritius OR Mayotte OR Mozambique OR Namibia OR Niger OR Nigeria OR Principe OR Reunion OR Rwanda OR "Sao Tome" OR Senegal OR Seychelles OR "Sierra Leone" OR "Saint Helena" OR Somalia OR "St Helena" OR "South Africa" OR "Southern Africa" OR Sudan OR Swaziland OR Tanzania OR Togo OR Uganda OR "Western Africa" OR "Western Sahara" OR Zaire OR Zambia OR Zimbabwe

Appendix IV: PRISMA 2020 Flow Diagram

PRISMA 2020 flow diagram for new systematic reviews which included searches of databases and registers only

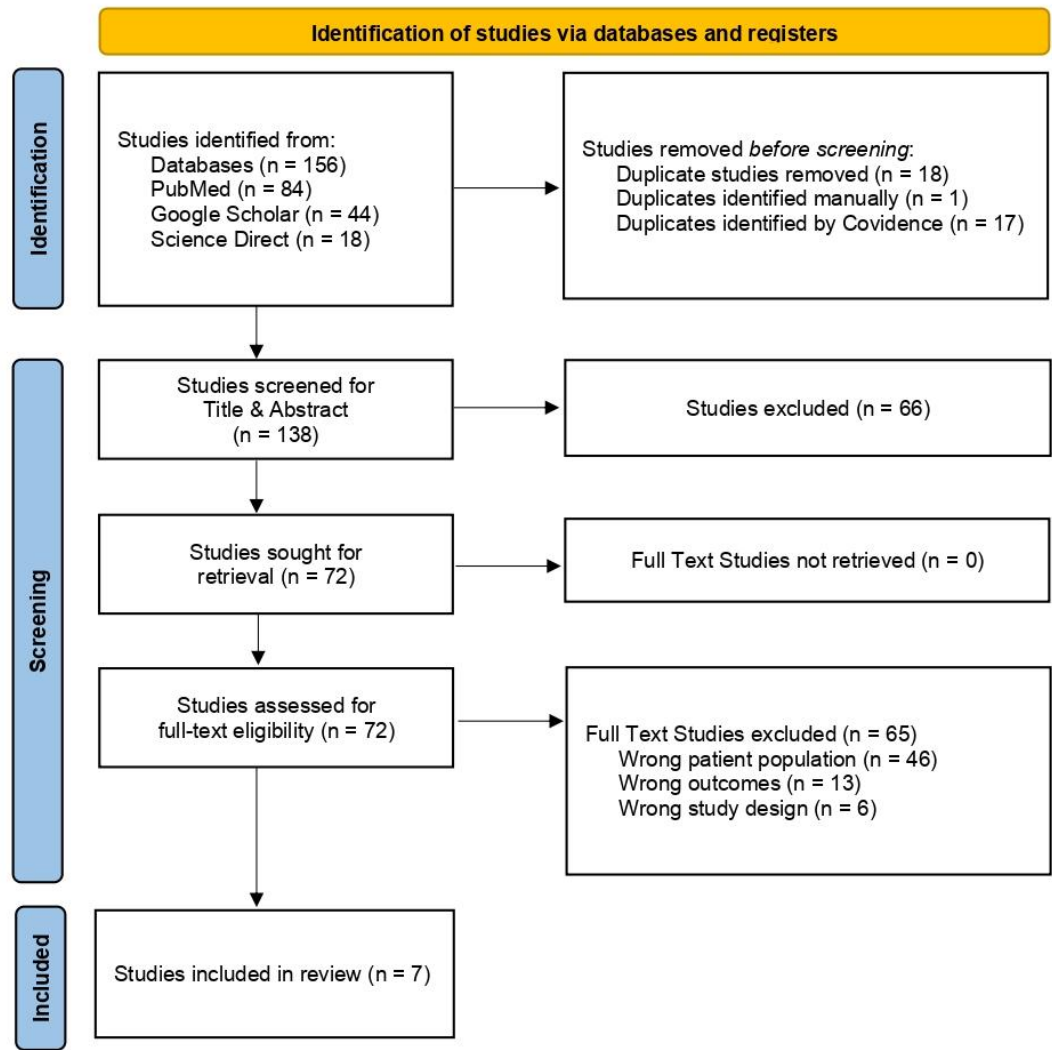


Figure 2: PRISMA Flow diagram outlining study selection process (57).

Appendix V: PRISMA 2020 checklist

Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) Checklist (59).

SECTION	ITEM	PRISMA-ScR CHECKLIST ITEM	REPORTED ON PAGE #
TITLE			
Title	1	Identify the report as a scoping review.	1
ABSTRACT			
Structured summary	2	Provide a structured summary that includes (as applicable): background, objectives, eligibility criteria, sources of evidence, charting methods, results, and conclusions that relate to the review questions and objectives.	3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known. Explain why the review questions/objectives lend themselves to a scoping review approach.	7
Objectives	4	Provide an explicit statement of the questions and objectives being addressed with reference to their key elements (e.g., population or participants, concepts, and context) or other relevant key elements used to conceptualize the review questions and/or objectives.	8
METHODS			
Protocol and registration	5	Indicate whether a review protocol exists; state if and where it can be accessed (e.g., a Web address); and if available, provide registration information, including the registration number.	35
Eligibility criteria	6	Specify characteristics of the sources of evidence used as eligibility criteria (e.g., years considered, language, and publication status), and provide a rationale.	9-10
Information sources*	7	Describe all information sources in the search (e.g., databases with dates of coverage and contact with authors to identify additional sources), as well as the date the most recent search was executed.	9
Search	8	Present the full electronic search strategy for at least 1 database, including any limits used, such that it could be repeated.	Table 3 & Table 4
Selection of sources of evidence†	9	State the process for selecting sources of evidence (i.e., screening and eligibility) included in the scoping review.	10-11 Table 1
Data charting process‡	10	Describe the methods of charting data from the included sources of evidence (e.g., calibrated forms or forms that have been tested by the team before their use, and whether data charting was done independently or in duplicate) and any processes for obtaining and confirming data from investigators.	11
Data items	11	List and define all variables for which data were sought and any assumptions and simplifications made.	11

SECTION	ITEM	PRISMA-ScR CHECKLIST ITEM	REPORTED ON PAGE #
Critical appraisal of individual sources of evidence§	12	If done, provide a rationale for conducting a critical appraisal of included sources of evidence; describe the methods used and how this information was used in any data synthesis (if appropriate).	11
Synthesis of results	13	Describe the methods of handling and summarizing the data that were charted.	11
RESULTS			
Selection of sources of evidence	14	Give numbers of sources of evidence screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally using a flow diagram.	11 Figure 1 & Figure 2
Characteristics of sources of evidence	15	For each source of evidence, present characteristics for which data were charted and provide the citations.	Table 5
Critical appraisal within sources of evidence	16	If done, present data on critical appraisal of included sources of evidence (see item 12).	N.A.
Results of individual sources of evidence	17	For each included source of evidence, present the relevant data that were charted that relate to the review questions and objectives.	14-18 Table 2 & Table 5
Synthesis of results	18	Summarize and/or present the charting results as they relate to the review questions and objectives.	13
DISCUSSION			
Summary of evidence	19	Summarize the main results (including an overview of concepts, themes, and types of evidence available), link to the review questions and objectives, and consider the relevance to key groups.	18-23
Limitations	20	Discuss the limitations of the scoping review process.	24
Conclusions	21	Provide a general interpretation of the results with respect to the review questions and objectives, as well as potential implications and/or next steps.	24-25
FUNDING			
Funding	22	Describe sources of funding for the included sources of evidence, as well as sources of funding for the scoping review. Describe the role of the funders of the scoping review.	26

JB1 = Joanna Briggs Institute; PRISMA-ScR = Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews.

* Where *sources of evidence* (see second footnote) are compiled from, such as bibliographic databases, social media platforms, and Web sites.

† A more inclusive/heterogeneous term used to account for the different types of evidence or data sources (e.g., quantitative and/or qualitative research, expert opinion, and policy documents) that may be eligible in a scoping review as opposed to only studies. This is not to be confused with *information sources* (see first footnote).

‡ The frameworks by Arksey and O'Malley (6) and Levac and colleagues (7) and the JB1 guidance (4, 5) refer to the process of data extraction in a scoping review as data charting.

§ The process of systematically examining research evidence to assess its validity, results, and relevance before using it to inform a decision. This term is used for items 12 and 19 instead of "risk of bias" (which is more applicable to systematic reviews of interventions) to include and acknowledge the various sources of evidence that may be used in a scoping review (e.g., quantitative and/or qualitative research, expert opinion, and policy document).

From: Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, et al. PRISMA Extension for Scoping Reviews (PRISMA-ScR): Checklist and Explanation. *Ann Intern Med*. 2018;169:467–473. doi: 10.7326/M18-0850.

Table 5. Summary of the key characteristics of included studies

Author(s)	Title	Year	Study location	Objectives/Aim	Study design	Study Population	Sample size(n)	Measure(s)	Outcome(s)	Main findings
Agaba, P. et al.	Factors associated with early menopause among women in Nigeria	2017	Nigeria	To determine the prevalence of early menopause (EM) and factors associated with it in a cohort of HIV-infected individuals and HIV-negative controls in Jos, Nigeria.	Cross sectional study	Women aged 40 years and above living with HIV with Western Blot laboratory confirmation of seropositive status at Jos University Teaching Hospital (JUTH) HIV outpatient clinic and HIV-negative controls from the general population. Women with oophorectomy history, nursing mothers, those too ill to participate, missing menstrual status data, and current hormonal contraception use history are excluded.	714	Early menarche (FMP <11 years), employment status, education, HIV status and duration, hepatitis C status, HAART use, high baseline viral load, baseline CD4+ cell count	Age at natural menopause 54.5 years	EM prevalence of 22.9% (95% CI 17.9–28.6%), higher among HIV-positive compared to HIV-negative women (27.9% [95% CI 1.22–34.2%] vs 2.7% [95% CI 0.1–14.2%], $p < 0.001$). HIV infection (adjusted odds ratio [AOR]: 10.95, 95% CI 1.39–86.33) and sexual activity (AOR: 2.37, 95% CI 1.24–4.52) associated with EM. Early menarche (AOR: 14.88, 95% CI 1.37–161.10) and sexual activity (AOR: 2.02, 95% CI 1.03–3.96) independently associated with EM. Baseline CD4+ cell count ($p = 0.06$) and viral load ($p = 0.15$) were similar among those with and without EM.
Agaba, P. et al.	Prevalence and predictors of severe menopause symptoms among HIV- positive and - negative Nigerian women	2017	Nigeria	To compare and assess the prevalence of menopause symptoms, identify predictors of severe menopause and its associated factors among women living with and without HIV in Jos, Nigeria.	Cross sectional study	Women aged between 40 and 80 years living with HIV with Western Blot laboratory confirmation of seropositive status at the HIV outpatient clinic of Jos University Teaching Hospital. Women who had undergone hysterectomy or oophorectomy, nursing mothers, or those too ill to participate due to comorbid conditions or a low Karnofsky score.	714	MRS WHOOQOL-BREF questionnaire	Frequency and severity of menopausal symptoms; predictors of severe menopause symptoms	Prevalent menopause symptoms include hot flushes (67.2%), joint and muscle discomfort (66.2%), physical or mental exhaustion (65.3%), heart discomfort (60.4%), anxiety (56.4%). HIV-positive status (AOR: 3.01, 95% CI: 1.20–7.54) and a history of cigarette smoking (AOR: 4.18, 95% CI: 1.31–13.26) associated with severe menopause symptoms. Symptoms status (AOR: 0.49, 95% CI: 0.32–0.77), premenopausal status (AOR: 0.60, 95% CI: 0.39–0.94), good QoL (AOR: 0.62, 95% CI: 0.39–0.98) protective factors against severe menopause symptoms.
Ellis, C. et al.	Factors Associated with Bone Mineral Density and Bone Resorption Markers in Postmenopausal HIV-Infected Women on Antiretroviral Therapy: A Prospective Cohort Study	2021	South Africa	To determine factors associated with changes in bone mineral density (BMD) and bone resorption markers over a two-year period in black postmenopausal women living with human immunodeficiency virus (HIV) and receiving antiretroviral therapy (ART).	Cohort	Postmenopausal HIV-infected women aged > 45 years on ART from Potchefstroom, South Africa Women with low BMD, secondary causes of osteoporosis, diabetes, metabolic bone disease, calcium and vitamin D supplementation, anti-acids, high alcohol consumption, and a fracture within the last six months are excluded.	120	DXA GPAQ Fracture risk was assessed using a checklist based on literature-derived information	BMD of the total body, lumbar spine and LFN of the hip, CTX and 25(OH)D	Total and LFN BMD increased significantly. Small or no changes in CTX. Decrease in serum vitamin D. No significant change in spine BMD over time was detected ($p = 0.19$, effect size = 0.02). Age significantly positively associated with CTX and negatively with total and LFN BMD. Physical activity (PA) positively associated with LFN BMD ($p = 0.008$).
Jeff, N. et al.	Staging reproductive aging Using Stages of Reproductive Aging Workshop + 10 in black urban African women in the Study of Women Entering and Endocrine Transition	2014	South Africa	To examine reproductive aging in urban African women by evaluating the applicability of the STRAW + 10 criteria in staging ovarian aging based on bleeding patterns. To determine if obesity influenced the menopausal transition (MT), final menstrual period (FMP), and menopausal symptoms, particularly vasomotor symptoms (VMS). To analyze if HIV infection was associated with age at FMP and menopausal symptoms in this population.	Cross sectional study	Black African Women aged 40–60 years living with HIV in the Birth to Twenty Plus cohort. Women older than 60 excluded.	702	STRAW + 10 criteria MRS	MT Stage, Menopausal status & symptoms, VMS severity, FSH levels, E2 level, HIV status, BMI, hormone therapy, tobacco and contraceptive use.	FMP was higher in women within 4 years of FMP (mean [SD], 49.0 [3.80] y) than in women 10 years or more after FMP (mean [SD], 42.0 [4.06] y; $P < 0.0005$). Lower BMI associated with earlier FMP age. Increased FSH levels, decreased estradiol levels. Menopausal symptoms were unaffected by HIV. Severe vasomotor symptoms were associated with obesity.
Madanhire, T. et al.	The Impact of Human Immunodeficiency Virus and Menopause on Bone Mineral Density: A Longitudinal Study of Urban-Dwelling South African Women	2023	South Africa	To assess changes in bone mineral density (BMD) in urban South African women with and without HIV during the menopausal transition. To assess if HIV infection modified the effect of menopause on BMD changes.	Cohort	Women aged 40–60 years living with HIV in Soweto. Women who had hysterectomy, used contraceptives or MHT, HIV-negative at baseline excluded.	504	DXA GPAQ Self-reported final menstrual cycle used categorized into one of three menopausal groups at baseline and follow-up (FMP).	Primary: TB, TH, and LS BMD (ABMD, g/cm2) changes Secondary: TBLH fat and fat-free (lean) mass changes.	Black HIV-positive South African women experience bone loss, particularly at the TB and LS, as they approach post menopause. Osteoporosis affects 13.6% of women aged ≥50 years and 25% of those with HIV. HIV prevalence among urban-dwelling women is slightly lower than rural-dwelling women with HIV in South Africa, with 37% having a T-score ≤ -2.5. The co-existence of HIV makes the loss worse, as HIV infection augments the effect of postmenopausal estrogen loss on bone. Losses in LS and TB BMD are approximately double those seen in women without HIV infection. Bone density is lower in those living with HIV compared to women without HIV. Living with HIV during menopause is associated with detrimental body composition changes, including a decrease in BMD and an increase in fat mass, with potential implications for future fracture and metabolic risks.
Madanhire, T. et al.	Menopausal symptoms by HIV status and association with health-related quality of life among women in Zimbabwe: a cross- sectional study	2023	Zimbabwe	To determine the prevalence and severity of self-reported menopause symptoms in Zimbabwean women at different stages of menopausal transition and determine how symptoms differ based on HIV status. To explore additional factors associated with menopausal symptoms and examine the relationship between menopausal symptoms and health-related quality of life (HROQL) in individuals with and without HIV.	Cross sectional study	Women aged 40–60 years living with HIV in Harare, Zimbabwe from the Sally Mugabe and Parrenyatiwa Hospitals HIV clinics. Women who were pregnant, severely ill, had undergone a hysterectomy or oophorectomy, failed to provide informed consent were excluded.	378	MRS WHOOQOL questionnaire GPAQ Shona symptom questionnaire	HROQL MRS score Comorbidities (tuberculosis, diabetes, hypertension, cardiac disease, arthritis, balance impairment).	WLHIV experienced more moderate (24.9% vs. 18.1%) and severe (9.7% vs. 2.6%) somatic & psychological menopause symptoms compared to women without HIV. 80.9% pre-menopausal women, 94.1% perimenopausal, 77.3% postmenopausal women had at least one menopausal symptom. HIV (OR: 2.02 [1.28, 3.21]), mood disorders (OR: 8.80 [2.77, 28.0]), 22 falls/year (OR: 2.16 [1.18, 15.6]), early menarche (OR: 2.33 [1.22, 4.48]), alcohol consumption (OR: 0.99, 2.46) associated with moderate/severe menopause symptoms. 25.4% of WLHIV reported moderate or severe psychological symptoms. Moderate or severe psychological symptoms were associated with higher MRS scores, highest frequency of symptoms, with 78% experiencing somatic and/or urogenital symptoms, and 69% psychological symptoms. With increasing severity of menopause symptoms, lower mean HROQL scores were observed. HIV modified the association with menopausal stage, somatic and psycho-logical symptoms
Obireasal, M. et al.	Menopause is associated with bone loss, particularly at the distal radius, in black South African women: Findings from the Study of Women Entering and in the Endocrine Transition (SWEET)	2022	South Africa	To evaluate trabecular and cortical bone compartments in women at various stages of the menopausal transition. To characterize bone density, geometry, and estimated strength in women based on their menopausal status. To explore whether variations in these patterns among women living with HIV and determine if HIV status modifies the association between menopause and bone outcomes.	Cross sectional study	Black African women aged 40–60 years living with HIV. Pregnant women excluded.	430	pOCT scans of the radius and tibia assessing various BMD, compressive bone strength, total CSA, cortical thickness, stress-strain index, and bone mineral density. CALCBP was used to calculate total cross-sectional area (CSA) and total and trabecular volumetric bone mineral density (vBMD).	pOCT outcomes (distal radius and tibia CSA, total volumetric BMD, compressive BMD, trabecular thickness, 33% the trabecular BMD, total CSA, cortical thickness).	Later menopause stage associated with lower 4 % radius total mean vBMD (post menopause: .330 [1.322; .737] 6) mg/cm3, $p = 0.017$) and BMD (post menopause: 0.36 [0.35; 0.37] g2/cm4; $p = 0.012$). 66 % radius for cortical vBMD (post menopause: 1136.1 [1130.1, 1142.0] mg/cm3; $p = 0.028$) and for trabecular vBMD (post menopause: 1136.9 [1128.5, 1177.2] mg/cm3; $p = 0.036$). Smaller radius vBMD (post menopause: 1123.6 [1108.0, 1141.2] mg/cm3, $p = 0.048$) in WLHIV postmenopause. Little variation in Total CSA by menopause or HIV status at either radius sites or tibia.

Abbreviations: vBMD-volumetric Bone Mineral Density; TB-Total body; LS-Lumbar Spine; LFN-Left Femoral Neck; BSIC-Bone Strength Index; MRS-Menopause Rating Scale; DXA-Dual energy X-ray Absorptiometry; GPAQ-Global Physical Activity Questionnaire; FMP-Final menstruation period; MT-Menopausal Transition; CSA-Cross- Sectional Area; WHOOQL- World Health Organisation Quality Of Life; HROQL-Health-related quality of life; PA-Physical activity; HAART-Highly Active Antiretroviral Therapy; BMI-Body Mass Index; ART-Antiretroviral therapy



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29 July 2024

HREC/REF: 590/2024

Prof Landon Myer

Public Health & Family Medicine

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Dear Prof Myer

PROJECT TITLE: MENOPAUSE EXPERIENCES AMONG WOMEN LIVING WITH HIV (WLHIV) IN SUB-SAHARAN AFRICA: A SCOPING REVIEW (MASTER'S IN PUBLIC HEALTH -EPIDEMIOLOGY AND BIOSTATISTICS CANDIDATE NOKWANDA THEMBA)

Thank you for submitting your study to the Faculty of Health Sciences Human Research Ethics Committee.

The HREC confirms that the above-mentioned proposed study is a scoping review.

As the scoping review involves published literature available through publicly accessible electronic databases, research ethics review and approval is not required.

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The HREC acknowledges that the Master's In Public Health -Epidemiology And Biostatistics Candidate Nokwanda Themba is also involved in this project.

Yours sincerely

Signed by candidate

PROFESSOR MARC BLOCKMAN

CHAIRPERSON FACULTY OF HEALTH SCIENCES HUMAN RESEARCH ETHICS COMMITTEE



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