Published in final edited form as:
J Assoc Nurses AIDS Care. 2012 May ; 23(3): 195–203. doi:10.1016/j.jana.2011.06.008.

Menopause-Associated Metabolic Manifestations and Symptomatology in HIV Infection: A Brief Review with Research Implications

Sara E. Dolan Looby, PhD, ANP-BC
Instructor in Medicine, Harvard Medical School, Program in Nutritional Metabolism, Massachusetts General Hospital, Boston, MA, USA

Abstract

Many women living with HIV in the United States have entered or will soon enter menopause. Clinical changes including increased visceral fat, reduced muscle mass, and changes in lipids and bone density are seen across the menopause transition among non-infected women. HIV and antiretroviral therapy (ART) use have been associated with similar manifestations, including reduced bone density, and changes in lipid metabolism and body composition. Menopause is also associated with changes in mood, quality of life, and vasomotor symptoms. Similar psychological indices are common among women with HIV, and may worsen during menopause transition. Research investigating the presence and acuity of metabolic, psychological, and vasomotor symptoms among perimenopausal women with HIV is limited. An important, yet unknown consideration for researchers and clinicians is how metabolic and psychological co-morbidities associated with HIV will influence changes associated with menopause in this population. Further research is needed to provide answers to these important questions.

Keywords

HIV; menopause; metabolic complications; women

Many women living with HIV in the United States have entered or will soon enter menopause (Fan, Maslow, Santoro, & Schoenbaum, 2008). At the end of 2007, approximately 146,692 women were living with HIV in the United States, and the greatest percentage of all infected individuals (men and women) were between the ages of 40-44 (Centers for Disease Control and Prevention, 2009). Additionally, the rate of new cases of HIV has increased among women ages 50 and older (Mack & Ory, 2003), reflecting a more mature profile of women living with the virus.

Clinical manifestations including increased visceral fat and waist circumference, reduced bone density, and increased cardiovascular risk, are observed during the menopause

Financial disclosure/conflict of interest: The author reports no real or perceived vested interests that relate to this article (including relationships with pharmaceutical companies, biomedical device manufacturers, grantors, or other entities whose products or services are related to topics covered in this manuscript) that could be construed as a conflict of interest. Dr. Looby reports having received honoraria from the Latino Health Institute, INC. and University of Massachusetts Worcester for speaking engagements on the metabolic effects of HIV presented to providers and consumers.

transition among women without HIV (Mesch et al., 2008; Sowers et al., 2006). Similarly, changes in body composition, reduced bone density, and alterations in lipid and glucose metabolism are common among women with HIV, and have been associated with the virus and potentially with antiretroviral therapy (ART) use as well (Dolan, Carpenter, & Grinspoon, 2007; Dolan et al., 2005; Rimland et al., 2006). However, whether HIV will influence or intensify such changes and lead to increased disease risk and symptomatology across the menopause transition, is unknown. Menopause is also associated with vasomotor symptoms and altered mood state, both of which can impact quality of life (Pinkerton & Zion, 2006; Soares, 2008). Indeed, depression and decreased quality of life are observed among women with HIV (Gore-Felton et al., 2006), and such symptoms may accelerate during the menopause transition.

Research investigating the presence and acuity of metabolic, psychological, and vasomotor symptoms among perimenopausal women with HIV is limited. An important, yet unknown consideration for both researchers and clinicians is how metabolic and psychological co-morbidities associated with the virus and its treatment will influence or exacerbate changes associated with menopause in this population. This paper will provide an overview of the metabolic and psychological manifestations associated with menopause, and how they relate to similar clinical indices associated with HIV.. It will also identify areas in need of further research among this population.

Literature Search

The literature search for this paper was conducted using the PubMed biomedical literature database. The purpose of the initial literature search was to identify clinical manifestations associated with menopause among women without HIV infection. The search generated a number of articles that identified conditions such as reduced bone density, increased cardiovascular risk, changes in body composition, vasomotor symptoms/hot flashes, and depression. Next, a search was conducted to identify articles published on HIV and menopause. The initial search terms included *HIV and menopause*, and *menopause symptoms and HIV*. This search generated a very limited number of articles including a few review articles that touched on metabolic challenges facing menopausal women with HIV. After a comprehensive review of the available literature was performed, more specific literature searches were conducted to further explore the HIV-related metabolic indices that overlie metabolic conditions associated with menopause including changes in body composition, reduced bone density, and increased cardiovascular risk. All literature was carefully reviewed and synthesized to meet the purpose of this paper.

Menopause-Associated Metabolic Manifestations

Changes in Body Composition

Changes in body composition including an increase in fat mass and waist circumference, as well as a decrease in skeletal muscle mass have been described among perimenopausal women without HIV (Sowers et al., 2007). In an investigation of body composition changes over 6 years among pre and perimenopausal women, Sowers and colleagues (2007) reported a cumulative increase of 3.4 kg of fat mass, a 5.7 cm increase in waist circumference, and a 0.23 kg reduction in skeletal mass among the HIV-uninfected women in their cohort. Changes in fat mass and waist circumference were associated with an increase in follicle stimulating hormone (FSH) levels (Sowers, et al., 2007). Indeed, changes in body composition, specifically an increase in visceral fat, have been associated with dyslipidemia, increased risk for cardiovascular disease, and insulin resistance (Guthrie et al., 2003).

Many HIV-infected individuals experience a similar pattern of fat redistribution, specifically an increase in truncal visceral adiposity and a decrease in subcutaneous fat and muscle mass, referred to as “lipodystrophy syndrome” (Grinspoon & Carr, 2005). Changes in body composition have been reported in approximately 40–50% of individuals with HIV (Grinspoon & Carr, 2005) and such changes, especially an increase in truncal adiposity, may pose additional risk for cardiovascular disease during the menopause transition.

Prior research by the Study of Fat Redistribution and Metabolic Change in HIV (FRAM, 2006) group has shown that abnormal fat distribution, characterized by peripheral lipoatrophy or an increase in truncal visceral adipose tissue (VAT), occurred more frequently among HIV-infected women than matched uninfected control subjects between the ages of 33-45 years. A disproportionate VAT: subcutaneous adipose tissue (SAT) ratio characterized by a decrease in SAT and an increase in VAT has been previously shown among a pre-menopausal age, race/ethnicity, and weight matched cohort of HIV-infected and uninfected subjects (Dolan, et al., 2005). Higher levels of total VAT have been associated with higher triglyceride levels and lower HDL levels among women with HIV (Currier et al., 2008). Similarly, a separate investigation among women in the Women’s Interagency HIV Study (mean age = 41-42 years) reported that waist to hip ratio (WHR) was significantly larger among women with HIV compared to the matched uninfected subjects (Justman et al., 2008).

Dyslipidemia, Alterations in Glucose Metabolism, & Cardiovascular Risk

Risk for cardiovascular disease (CVD) increases during the menopause transition and a number of factors, including loss of the protective effects of estrogen, contribute to this risk. Atherogenic changes in lipid profiles such as increased low density lipoprotein (LDL), apoprotein B and total cholesterol have been observed among peri- and post-menopausal women, and have been independently associated with menopause, age, and increased abdominal fat (Berg et al., 2004). In addition, reduced high density lipoprotein levels (HDL) are often observed during the menopause transition (Woodard et al., 2010). As previously mentioned, dyslipidemia may occur as a result of increased abdominal fat accumulation, further contributing to the abnormal metabolic state characterizing menopause (Guthrie et al., 2003). Insulin resistance in relation to androgen levels and an increase in abdominal fat have also been observed among women in the menopause transition (Mesch et al., 2008). In addition, smoking is an important risk factor for CVD that contributes further risk in the presence of hyperlipidemia and increased central adiposity.

Studies published in the post-combination ART era suggest that individuals with HIV are at increased risk for CVD. A number of metabolic complications including reduced HDL and increased LDL cholesterol, insulin resistance, and increased central adiposity have been described (Hadigan et al., 2001). The etiology of cardiovascular manifestations has been attributed to multiple factors including specific ART medications and/or drug classes, inflammatory effects of HIV, and traditional risk factors, including dyslipidemia (Boccara, 2008). In addition, modifiable risk factors for CVD such as decreased fitness and smoking are common in this population (Dolan et al., 2006; Tashima, 2009). Recent studies suggest that individuals with HIV may be at increased risk for myocardial infarction (MI). Findings from a large multi-cohort study known as the Data Collection on Adverse Events of Anti-HIV Drugs (D:A:D) study demonstrated that risk for MI increased in relation to duration of ART use (Friis-Moller et al., 2003). In addition, a recent study from a large patient data registry comprised of men and women with and without HIV showed that acute MI rates per 1000 person-years were increased in HIV-infected subjects compared to uninfected controls (11.13, 95% CI 9.58-12.68 vs. 6.98, 95% CI 6.89-7.06) and this difference was significant (RR = 1.75, $p < .0001$), adjusting for age, gender, race, and comorbidities including hypertension, diabetes, and dyslipidemia (Triant, Lee, Hadigan, & Grinspoon, 2007). A

separate analysis among the female subjects in this cohort demonstrated that the unadjusted acute MI rates were higher among women with HIV compared to women without HIV ($p < .0001$), and that the rate increased considerably with age, suggesting age was a co-factor. The HIV-infected individuals in the study also had higher rates of hypertension, diabetes, and dyslipidemia compared to the non-infected controls ($p < .0001$; Triant et al., 2007).

A limited number of studies have reported on risk for CVD exclusively among women with HIV. Among a cohort of predominately premenopausal HIV-infected and uninfected women matched by age, race/ethnicity, and weight, women with HIV had significantly higher triglyceride, C-reactive protein (CRP), insulin, and interleukin-6 levels, and lower HDL and adiponectin levels compared to the controls (Dolan et al., 2005). Other studies among women with HIV have shown an increased prevalence of the metabolic syndrome compared to control subjects (Sobieszczyk et al., 2008), and increased carotid intimal medial thickness among women treated with a protease inhibitor (Johnsen et al., 2006).

Reduced Bone Density

The menopause transition is associated with increased bone turnover and bone loss that can ultimately lead to fracture (Akhter, Lappe, Davies, & Recker, 2007). Although osteoporosis and osteopenia are more prevalent among postmenopausal women, bone loss has been documented among women in late perimenopause and early postmenopause (Finkelstein et al., 2008). A recent study among women without HIV in the Study of Women's Health Across the Nation (SWAN) cohort found that bone mineral density (BMD) decreased in late perimenopause (mean loss = 0.018 and 0.010 $g/cm^2/yr$, $p < .001$) at the hip and spine, and bone loss at a similar rate continued into early postmenopause (Finkelstein et al., 2008). Factors associated with bone loss among menopausal women vary in the literature. Lower body weight and smoking have been associated with increased bone loss among women in this population (Finigan et al., 2008; Finkelstein et al., 2008). Estrogen deficiency is strongly related to lower BMD, and Sowers and colleagues (2006) demonstrated that BMD loss at the hip and spine was related to the interaction between baseline and longitudinal FSH changes among women in the SWAN.

Low BMD has been described among men and women living with HIV in the era of combination ART, posing increased risk for fracture. Findings from a population-based cohort comprised of both HIV-infected and uninfected men and women from a large patient registry demonstrated that fracture prevalence was higher among the HIV-infected subjects compared to the matched uninfected control subjects (2.87 vs. 1.77 per 100 persons, $p < .0001$; (Triant, Brown, Lee, & Grinspoon, 2008). Fracture prevalence remained high among HIV-infected women compared to uninfected female control subjects in this cohort when the data were analyzed by gender ($p = .002$; Triant et al., 2008).

A limited number of studies have investigated BMD exclusively among HIV-infected women. Research among a cohort of 84 HIV-infected women compared to age, race/ethnicity, and weight matched uninfected controls ($n = 63$) showed that osteopenia was prevalent in 54% of the HIV-infected subjects versus 30% of the uninfected control subjects ($p = .004$), and women with HIV were 2.5 times more likely to have osteopenia in a multivariate analysis controlling for age, body mass index (BMI), and menstrual status (Dolan et al., 2004). In addition to reduced BMD, the HIV-infected women in this study demonstrated increased bone turnover and resorption compared to control subjects. Factors associated with reduced BMD in this cohort included BMI, history of low adult weight, lower fat and lean body mass, and increased urine *N*-telopeptide levels. BMD was also lower among women with FSH levels greater than 15 IU/L, and did not differ based on current or prior use of ART (Dolan et al., 2004). The etiology of reduced bone density among individuals with HIV is not definitive, although it has been shown to be related to

metabolic risk factors in this population. Brown and colleagues (2004) demonstrated reduced BMD among HIV-infected women and men related to increased central adiposity and post-load hyperglycemia. Findings also concluded that bone resorption was independently associated with dyslipidemia and female gender in this cohort.

Menopause-Associated Symptoms

Psychological Manifestations

Many women experience changes in mood state and increased risk for depression during the menopause transition, and these changes are often associated with hormone fluctuations (Utian, 2005). A longitudinal study among women in the menopause transition demonstrated that elevated scores on the Center for Epidemiologic Studies Depression Scale were more than 4 times more likely to occur during the perimenopause versus premenopause phase (Freeman, Sammel, Lin, & Nelson, 2006). A separate longitudinal study reported a significant increase in depression symptoms during the menopause transition that decreased in the postmenopause phase, documented by increased FSH levels ($p \leq .001$; Freeman et al., 2004). These findings remained significant when adjusted for history of depression, severe premenstrual syndrome, poor sleep, hot flashes, age, race, and employment status ($p = .03$; Freeman, et al., 2004). New onset of depression among women with no prior history of depression may occur among those who enter menopause earlier (Cohen, Soares, Vitonis, Otto, & Harlow, 2006), and having a history of depression has been shown to result in potentially early transition into menopause (Harlow, Wise, Otto, Soares, & Cohen, 2003).

It has been reported that one-third to one-half of men and women living with HIV experience symptoms of depression (Eller et al., 2005). Depression may occur after diagnosis of HIV, although some individuals may already have a history of depression prior to knowing their HIV status, putting them at risk for further development of depression symptoms (Penzak, Reddy, & Grimsley, 2000). Other stressors experienced by individuals living with acute or chronic illness include financial, family, relationship, and health-related concerns.

Psychosocial changes are common during the menopause transition, and such changes affect quality of life (QOL; Chedraui, San Miguel, & Avila, 2009). QOL reflects an individual's sense of well-being and satisfaction with daily life, relationships, and feeling of wellness (Utian, Janata, Kingsberg, Schluchter, & Hamilton, 2002). Decreased QOL is often related to the presence of vasomotor symptoms associated with the menopause transition including hot flashes, problems with sleeping, and depressed mood/irritability among this population (Utian, 2005).

Individuals living with HIV also experience reduced QOL. HIV has become a less acute and more chronic disease for many in the United States, and stressors associated with living with HIV including poor virologic control and low CD4+ T cell count can result in deceased QOL (Jia et al., 2007). In addition, QOL has been shown to be a strong predictor of depression among individuals with HIV (Gore-Felton et al., 2006).

Vasomotor, Genitourinary Symptoms, and Sleep Disturbance

Many women experience vasomotor and genitourinary symptoms, as well as sleep disturbance during the menopause transition. Vasomotor symptoms result from changes in levels of gonadal hormones during the menopause transition, and the presence and intensity often correspond with stage of menopause: pre, peri, or post (Martin & Manson, 2008; Pinkerton & Zion, 2006). Hot flashes have been described as the most prominent symptom (Pinkerton & Zion, 2006) and can vary with regard to frequency and intensity (Utian, 2005). Vaginal atrophy is another symptom that can lead to vaginal dryness and itching (Martin &

Manson, 2008). Sleep disturbances including insomnia, sleep apnea, and restless leg syndrome have also been described among menopausal women, although the etiology of these disturbances may be a mix of hormonal changes, hot flashes, and/or depressive symptoms (Martin & Manson, 2008; Pinkerton & Zion, 2006; Utian, 2005).

Vasomotor symptoms associated with the menopause transition including night sweats, sleep disturbances, and restless leg syndrome have also been associated with HIV infection (Happe, Kundmuller, Reichelt, Husstedt, & Evers, 2007; Hudson, Portillo, & Lee, 2008; Kojic, Wang, & Cu-Uvin, 2007), although few studies have been published on the presence of these symptoms among menopausal women with HIV. One investigation reported a higher prevalence of hot flashes and vaginal dryness among HIV-infected women compared to women without HIV based on the literature (Fantry, Zhan, Taylor, Sill, & Flaws, 2005). Ferreira and colleagues (2007) reported similar findings among a cohort of women with and without HIV, and found that menopause symptoms were more common among the HIV-infected women (specifically vasomotor, psychological, genitourinary, and insomnia symptoms: $p < .05$), and HIV infection was independently associated with menopause symptoms.

Implications for Future Research

Pre-menopausal women with HIV may experience metabolic and psychological manifestations related to the virus that are similar to clinical conditions and symptoms observed during the menopause transition. Given the potential for added disease risk in this population, there is a great need for research investigating the independent effect of HIV and/or ART on co-morbidities and symptoms associated with the menopause transition, and how metabolic co-morbidities associated with the virus will influence or intensify these changes. A variety of research methods should be implemented to evaluate clinical changes related to menopause and to capture the experience of menopause among women with HIV.

Further research is needed to evaluate the degree of excess visceral adiposity among perimenopausal women with HIV and the role VAT may play in contributing to increased inflammation and CVD risk among this population. In addition, little is known regarding patterns of lipid and glucose abnormalities among perimenopausal women with HIV, and the role the virus and/or ART plays as a unique contributing factor for CVD risk in this population. There is a paucity of literature with respect to data on bone mineral density among HIV-infected women during the menopause transition. Such data would offer insight into the prevalence of osteopenia, osteoporosis, and the potential for accelerated bone turnover and increased fracture risk among perimenopausal women with HIV.

Transition into menopause is associated with changes in mood state and vasomotor symptoms, both of which can lead to impaired QOL. Very little is known concerning the presence and severity of depressive symptoms or QOL among HIV-infected women during the menopause transition. In addition, research has suggested that women with HIV may experience a higher prevalence of vasomotor symptoms including hot flashes and vaginal dryness, both of which can lead to impaired QOL, although these studies are limited.

Nurses are in a pivotal position to provide answers to these important research questions. Findings from such studies would assist with guideline development for the assessment of CVD and fracture risk among perimenopausal women with HIV and inform the development and investigation of strategies to improve visceral fat accumulation in this population. An investigation of psychological and vasomotor symptoms associated with menopause among perimenopausal women with HIV would shed light on the importance of assessment and treatment of such conditions in this population, and offer insight into strategies to improve quality of life. Collectively, research findings would allow clinicians to

provide informed and comprehensive care to the growing number of maturing women with HIV as they approach menopause.

Acknowledgments

Sara E. Dolan Looby's current research is supported by the National Institute of Nursing Research grant # 1K23NR011833-01A1.

References

Akhter MP, Lappe JM, Davies KM, Recker RR. Transmenopausal changes in the trabecular bone structure. Bone. 2007 doi:10.1016/j.bone.2007.03.019.

Berg G, Mesch V, Boero L, Sayegh F, Prada M, Royer M, Benencia H. Lipid and lipoprotein profile in menopausal transition: Effects of hormones, age and fat distribution. Hormone Metabolism Research. 2004; 36(4):215–220. doi:10.1055/S-2004-814450.

Boccara F. Cardiovascular complications and atherosclerotic manifestations in the HIV-CR infected population: Type, incidence and associated risk factors. AIDS. 2008; 22(Suppl. 3):S19–S26. doi: 10.1097/01.aids.0000327512.76126.6e. [PubMed: 18845918]

Brown TT, Ruppe MD, Kassner R, Kumar P, Kehoe T, Dobs AS, Timpone J. Reduced bone mineral density in human immunodeficiency virus-infected patients and its association with increased central adiposity and postload hyperglycemia. Journal of Clinical Endocrinology and Metabolism. 2004; 89(3):1200–1206. doi:10.1210/jc.2003-031506. [PubMed: 15001610]

Centers for Disease Control and Prevention. HIV/AIDS Surveillance Report, 2007. 2009. Retrieved from http://www.cdc.gov/hiv/topics/surveillance/resources/reports/2007report/pdf/2007SurveillanceReport.pdf

Chedraui P, San Miguel G, Avila C. Quality of life impairment during the female menopausal transition is related to personal and partner factors. Gynecology Endocrinology. 2009; 25(2):130–135. doi:10.1080/09513590802617770.

Cohen LS, Soares CN, Vitonis AF, Otto MW, Harlow BL. Risk for new onset of depression during the menopausal transition: The Harvard study of moods and cycles. Archives of General Psychiatry. 2006; 63(4):385–390. doi:10.1001/archpsyc.63.4.385. [PubMed: 16585467]

Currier J, Scherzer R, Bacchetti P, Heymsfield S, Lee D, Sidney S, Tien PC. Regional adipose tissue and lipid and lipoprotein levels in HIV-infected women. Journal of Acquired Immune Deficiency Syndrome. 2008; 48(1):35–43. doi:10.1097/QAI.0b013e318164227f.

Dolan SE, Carpenter S, Grinspoon S. Effects of weight, body composition, and testosterone on bone mineral density in HIV-infected women. Journal of Acquired Immune Deficiency Syndrome. 2007; 45(2):161–167. doi:10.1097/QAI.0b013e31804a7f4d.

Dolan SE, Frontera W, Librizzi J, Ljungquist K, Juan S, Droman R, Grinspoon S. The effects of a supervised home-based aerobic and progressive resistance training regimen in HIV-infected women: randomized trial. Archives of Internal Medicine. 2006; 166:1225–1231. [PubMed: 16772251]

Dolan SE, Hadigan C, Killilea KM, Sullivan MP, Hemphill L, Lees RS, Grinspoon S. Increased cardiovascular disease risk indices in HIV-infected women. Journal of Acquired Immune Deficiency Syndromes. 2005; 39(1):44–54. [PubMed: 15851913]

Dolan SE, Huang JS, Killilea KM, Sullivan MP, Aliabadi N, Grinspoon S. Reduced bone density in HIV-infected women. AIDS. 2004; 18(3):475–483. doi:10.1097/01.aids.0000111394.02002.e1. [PubMed: 15090800]

Eller LS, Corless I, Bunch EH, Kemppainen J, Holzemer W, Nokes K, Nicholas P. Self-care strategies for depressive symptoms in people with HIV disease. Journal of Advanced Nursing. 2005; 51(2): 119–130. doi:10.1111/j.1365-2648.2005.03474.x. [PubMed: 15963183]

Fan MD, Maslow B-S, Santoro N, Schoenbaum E. HIV and the menopause. Menopause International. 2008; 14(4):163–168. doi:10.1258/mi.2008.008027. [PubMed: 19037065]

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; 19(11):703–711. doi:10.1089/apc.2005.19.703. [PubMed: 16283830]

Ferreira CE, Pinto-Neto AM, Conde DM, Costa-Paiva L, Morais SS, Magalhaes J. Menopause symptoms in women infected with HIV: Prevalence and associated factors. Gynecology Endocrinology. 2007; 23(4):198–205. doi:10.1080/09513590701253743.

Finigan J, Greenfield DM, Blumsohn A, Hannon RA, Peel NF, Jiang G, Eastell R. Risk factors for vertebral and nonvertebral fracture over 10 years: A population-based study in women. Journal of Bone Mineral Research. 2008; 23(1):75–85. doi:10.1359/jbmr.070814.

Finkelstein JS, Brockwell SE, Mehta V, Greendale GA, Sowers MR, Ettinger B, Neer RM. Bone mineral density changes during the menopause transition in a multiethnic cohort of women. Journal of Clinical Endocrinology and Metabolism. 2008; 93(3):861–868. doi:10.1210/jc.2007-1876. [PubMed: 18160467]

Freeman EW, Sammel MD, Lin H, Nelson DB. Associations of hormones and menopausal status with depressed mood in women with no history of depression. Archives of General Psychiatry. 2006; 63(4):375–382. doi:10.1001/archpsyc.63.4.375. [PubMed: 16585466]

Freeman EW, Sammel MD, Liu L, Gracia CR, Nelson DB, Hollander L. Hormones and menopausal status as predictors of depression in women in transition to menopause. Archives of General Psychiatry. 2004; 61(1):62–70. [PubMed: 14706945]

Friis-Moller N, Sabin CA, Weber R, d'Arminio Monforte A, El-Sadr WM, Reiss P, Lundgren JD. Combination antiretroviral therapy and the risk of myocardial infarction. New England Journal of Medicine. 2003; 349(21):1993–2003. doi:10.1056/NEJMoa030218. [PubMed: 14627784]

Gore-Felton C, Koopman C, Spiegel D, Vosvick M, Brondino M, Winningham A. Effects of quality of life and coping on depression among adults living with HIV/AIDS. Journal of Health Psychology. 2006; 11(5):711–729. doi:10.1177/1359105306066626. [PubMed: 16908468]

Grinspoon S, Carr A. Cardiovascular risk and body fat abnormalities in HIV-infected adults. New England Journal of Medicine. 2005; 352(1):48–62. [PubMed: 15635112]

Guthrie JR, Dennerstein L, Taffe JR, Ebeling PR, Randolph JF, Burger HG, Wark JD. Central abdominal fat and endogenous hormones during the menopausal transition. Fertility and Sterility. 2003; 79(6):1335–1340. doi:10.1016/S0015-0282(03)00361-3. [PubMed: 12798880]

Hadigan C, Meigs JB, Corcoran C, Rietschel P, Piecuch S, Basgoz N, Grinspoon S. Metabolic abnormalities and cardiovascular disease risk factors in adults with human immunodeficiency virus infection and lipodystrophy. Clinical Infectious Diseases. 2001; 32(1):130–139. doi:10.1086/317541. [PubMed: 11118392]

Happe S, Kundmuller L, Reichelt D, Husstedt IW, Evers S. Comorbidity of restless legs syndrome and HIV infection. Journal of Neurology. 2007; 254(10):1401–1406. doi:10.1007/s00415-007-0563-2. [PubMed: 17934881]

Harlow BL, Wise LA, Otto MW, Soares CN, Cohen LS. Depression and its influence on reproductive endocrine and menstrual cycle markers associated with perimenopause: The Harvard Study of Moods and Cycles. Archives of General Psychiatry. 2003; 60(1):29–36. [PubMed: 12511170]

Hudson AL, Portillo CJ, Lee KA. Sleep disturbances in women with HIV or AIDS: Efficacy of a tailored sleep promotion intervention. Nursing Research. 2008; 57(5):360–366. doi:10.1097/01.NNR.0000313501.84604.2c. [PubMed: 18794720]

Jia H, Uphold CR, Zheng Y, Wu S, Chen GJ, Findley K, Duncan PW. A further investigation of health-related quality of life over time among men with HIV infection in the HAART era. Quality of Life Research. 2007; 16(6):961–968. doi:10.1007/s11136-007-9214-4. [PubMed: 17468942]

Johnsen S, Dolan SE, Fitch KV, Kanter JR, Hemphill LC, Connelly JM, Grinspoon S. Carotid intimal medial thickness in HIV infected women: Effects of protease inhibitor use, cardiac risk factors and the metabolic syndrome. Journal of Clinical Endocrinology and Metabolism. 2006; 91(12):4916–24. doi:10.1210/jc.2006-1140. [PubMed: 17003092]

Justman JE, Hoover DR, Shi Q, Tan T, Anastos K, Tien PC, Grinspoon S. Longitudinal anthropometric patterns among HIV-infected and HIV-uninfected women. Journal of Acquired Immune Deficiency Syndrome. 2008; 47(3):312–319. doi:10.1097/QAI.0b013e318162f597.

Kojic EM, Wang CC, Cu-Uvin S. HIV and menopause: A review. Journal of Womens Health. 2007; 16(10):1402–1411. doi:10.1089/jwh.2007.0345.

Mack KA, Ory MG. AIDS and older Americans at the end of the twentieth century. Journal of Acquired Immune Deficiency Syndrome. 2003; 33(Suppl 2):S68–S75.

Martin KA, Manson JE. Approach to the patient with menopausal symptoms. Journal of Clinical Endocrinology and Metabolism. 2008; 93(12):4567–4575. doi:10.1210/jc.2008-1272. [PubMed: 19056840]

Mesch VR, Siseles NO, Maidana PN, Boero LE, Sayegh F, Prada M, Berg GA. Androgens in relationship to cardiovascular risk factors in the menopausal transition. Climacteric. 2008; 11(6): 509–517. doi:10.1080/13697130802416640. [PubMed: 18991078]

Penzak SR, Reddy YS, Grimsley SR. Depression in patients with HIV infection. American Journal of Health-Systems Pharmacy. 2000; 57(4):376–3869.

Pinkerton JV, Zion AS. Vasomotor symptoms in menopause: Where we've been and where we're going. Journal of Womens Health. 2006; 15(2):135–145. doi:10.1089/jwh.2006.15.135.

Rimland D, Guest JL, Hernandez-Ramos I, Del Rio C, Le NA, Brown WV. Antiretroviral therapy in HIV-positive women is associated with increased apolipoproteins and total cholesterol. Journal of Acquired Immune Deficiency Syndrome. 2006; 42(3):307–313. doi:10.1097/01.qai.0000220164.72113.12.

Soares CN. Practical strategies for diagnosing and treating depression in women: Menopausal transition. Journal of Clinical Psychiatry. 2008; 69(10):e30. [PubMed: 19192433]

Sobieszczyk ME, Hoover DR, Anastos K, Mulligan K, Tan T, Shi Q, Justman J. Prevalence and predictors of metabolic syndrome among HIV-infected and HIV-uninfected women in the Women's Interagency HIV Study. Journal of Acquired Immune Deficiency Syndrome. 2008; 48(3):272–280. doi:10.1097/QAI.0b013e31817af461.

Sowers MR, Jannausch M, McConnell D, Little R, Greendale GA, Finkelstein JS, Ettinger B. Hormone predictors of bone mineral density changes during the menopausal transition. Journal of Clinical Endocrinology and Metabolism. 2006; 91(4):1261–1267. doi:10.1210/jc.2005-1836. [PubMed: 16403818]

Sowers M, Zheng H, Tomey K, Karvonen-Gutierrez C, Jannausch M, Li X, Symons J. Changes in body composition in women over six years at midlife: Ovarian and chronological aging. Journal of Clinical Endocrinology and Metabolism. 2007; 92(3):895–901. doi:10.1210/jc.2006-1393. [PubMed: 17192296]

Study of Fat Redistribution and Metabolic Change in HIV Infection (FRAM). Fat distribution in women with HIV infection. Journal of Acquired Immune Deficiency Syndromes. 2006; 42(5): 562–571. doi:10.1097/01.qai.0000229996.75116.da. [PubMed: 16837863]

Tashima, KT.; Niaura, R.; Richardson, E.; Stanton, C.; De Dios, M.; Kojic, M. Positive Paths: A motivational intervention for smoking cessation among HIV positive smokers: Oral Abstract Presentation; Paper presented at the 16th Conference on Retroviruses and Opportunistic Infections; Montreal, Canada. 2009, February;

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. Journal of Clinical Endocrinology and Metabolism. 2008; 93(9):3499–3504. doi:10.1210/jc.2008-0828. [PubMed: 18593764]

Triant VA, Lee H, Hadigan C, Grinspoon SK. Increased acute myocardial infarction rates and cardiovascular risk factors among patients with human immunodeficiency virus disease. Journal of Clinical Endocrinology and Metabolism. 2007; 92(7):2506–2512. doi:10.1210/jc.2006-2190. [PubMed: 17456578]

Utian WH. Psychosocial and socioeconomic burden of vasomotor symptoms in menopause: A comprehensive review. Health Quality of Life Outcomes. 2005; 3:47. doi: 10.1186/1477-7525-3-47.

Utian WH, Janata JW, Kingsberg SA, Schluchter M, Hamilton JC. The Utian Quality of Life (UQOL) Scale: development and validation of an instrument to quantify quality of life through and beyond menopause. Menopause. 2002; 9(6):402–410. doi:10.1097/01.GME.0000033609.60079.71. [PubMed: 12439099]

Woodard GA, Brooks MM, Barinas-Mitchell E, Mackey RH, Matthews KA, Sutton-Tyrrell K. Lipids, menopause, and early atherosclerosis in Study of Women's Health Across the Nation Heart women. Menopause. 2010 doi:10.1097/gme.0b013e3181f6480e.