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REVIEW ARTICLE

Understanding the menopause journey

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ABSTRACT

The menopause experience is unique to people with ovaries who attain an age at which functioning follicles are depleted. Unlike male reproductive aging, menopause is accompanied by a definable reproductive milestone in that menstrual periods cease and the failure of follicle growth results in a large drop in circulating estrogen and no further ovarian production of progesterone. While the focus on menopause has largely been centered on this absence of hormone production, the most dynamic changes in symptoms and health markers begin before the final menstrual period, and merit attention. Vasomotor symptoms, the most common symptom of menopause and the primary symptom that drives women to seek treatment, peak in frequency and prevalence in the late menopause transition, when women are still having menstrual periods. Body composition and adverse lipoprotein and lipid changes also worsen most acutely in the late transition, and then assume a slower, age-related trajectory of change. Multiple processes that worsen across the transition restabilize after it is over. The notion that the menopause transition is an adaptive process for women has scientific merit and suggests that facilitating this adaptation and recognizing its implications may represent the next phase of progress in the field.

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Introduction

Menopause is having 'a moment'. The lay press and social media are alight with information, advice and marketing of (often) untested products to treat this natural life transition [1]. A 'new' movement is afoot dedicated to eliminating menopause by preserving ovarian function into older adulthood [2]. In recognition of the detrimental impact that menopause, and the menopause transition (MT) in particular, can have on women's careers, the UK's Women and Equalities Committee (WEC) provided the government with a report on 'Menopause and the Workplace' that contained recommendations to include menopause as a protected characteristic and to pilot a menopause leave policy in collaboration with large employers. Ultimately, Parliament rejected making any new sweeping regulations and left policy up to individual employers [3].

These developments indicate both promise and peril for those who provide healthcare for women in their perimenopausal and postmenopausal years. Most worldwide clinical guidelines agree that menopausal women who are symptomatic and have no contraindications to their use have a favorable benefit-to-risk profile with hormone therapy. There are also a host of non-hormonal treatments, some now government approved, to help those who cannot or do not wish to use hormone therapy to treat their symptoms. However, many non-evidence-based clinical practices are widely advertised on social media and have gained popularity despite specific recommendations and evidence against their use, such as hormone pellets and compounded treatments, which are not recommended and have been shown to cause harm [4, 5] yet are widespread and have numerous, enthusiastic social media followers. Directing patients to appropriate treatment can therefore be challenging.

A second, important challenge lies in the appropriate timing of treatment. Most menopausal symptoms are at their worst during the late MT, when women have prolonged amenorrhea for >60 days but have not yet gone a full year without a menstrual period [6]. Hormone therapy at this time of life can be complicated by the concurrent need for contraception and the risk of breakthrough bleeding with traditional menopausal hormone treatments. However, emerging evidence, which will be covered in detail in this review, indicates that multiple markers of future health and disease also acutely worsen in the late MT. This worsening may be a herald of future disease risk for any individual woman, which can be averted by instituting standard preventive measures. This timing supports the MT as a life transition when a woman can and should take stock of her overall health and proactively manage her health risks. On the other hand, it is also possible that the acute perturbations of the MT, if treated promptly, may avert adverse downstream health consequences.

This review will describe the hormonal processes that characterize the MT and the concurrent symptoms associated with its stages. Longer-term individual trajectories of change

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in key symptoms and their implications for future health will also be discussed. Processes such as bone resorption, which accelerates in the perimenopausal years (a period of 2–5 years transected by the final menstrual period [FMP]) but then subsides, will be differentiated from processes that seem to involve a permanent 'resetting' of incidence (such as metabolic syndrome) beginning in the late MT.

The hormonal processes that lead to menopause are highly variable

The early MT

A number of longitudinal epidemiological studies of the MT over the past three decades have provided invaluable information on the nature of the transition [7–10]. Burger et al. were the first to describe the critical role of the shrinkage of the ovarian follicle cohort as the inciting event that initiates the MT [11]. As the ovarian reserve approaches a critical level, the restraint on follicle stimulating hormone (FSH) exerted by the inhibins, products of small and growing follicles, is reduced. This loss of FSH inhibition leads to rapid follicle growth, with evidence of excessive estradiol production in some cases [12], and maturation of the next cycle's dominant follicle in the preceding cycle's luteal phase [13]. These processes result in less predictable menstrual cycles, and when the available follicles in a particular cycle are insufficient, a menstrual period is skipped. Mathematical modeling of the MT can predict these changing patterns as a function of the overall ovarian follicle reserve [14]. At this point in the MT, estradiol levels are not overall reduced, but they are certainly more variable. It is at this point in the transition that symptoms begin to increase. Others have theorized that there is a phase or phases that precede the transition called the late reproductive stage [6, 15, 16]. Symptoms associated with the late reproductive stage are similar but not identical to those of the MT. It is likely that ovarian aging is a continuum, and women may present with symptoms earlier than their mid to late 40s; however, clear-cut clinical definitions are lacking, as is evidence for optimal treatments for the late reproductive stage. Given that the hormonal changes of the early MT include wider excursions of estradiol (and possibly progesterone), treatments designed to provide more stable circulating hormone levels, such as continuous combined hormonal contraception, may be the most effective. As menstrual cycles (and ovulation) are frequent in the early MT, contraceptive needs may often drive treatment options.

The late MT

By the late MT, follicle reserve has become critically low and prolonged amenorrhea of at least 60 days and less than 365 days has occurred. Circulating estradiol is notably lower, less progesterone appears to be produced when cycles do occur and intermittent periods of very low estradiol occur [17–19]. It is at this point in the transition that women report the largest increase in prevalence of typical menopausal symptoms. Treatments designed to minimize prolonged hypoestrogenemia while also providing stable hormone levels are most effective at this point in the MT. While menstrual cycles are less frequent, ovulation may still occur and contraception must be considered. However, excellent symptom relief can be achieved with standard hormone therapy dosing, and the relatively infrequent menstrual cycles in the late transition make breakthrough bleeding less of a problem.

Patterns of change over time and their implications

The patterns of hormone changes over the transition include a rise in FSH and a decrease of estradiol, of course, but the rate of change of these two hormones is impacted by several characteristics. Obesity is related to a 'flatter' trajectory of estradiol decline. In other words, circulating estradiol is lower in women with obesity early in the MT, and after the FMP remains higher than in women without obesity, the latter likely due to extraglandular conversion of precursors to estrogens [20]. Reciprocal changes in FSH follow a flatter trajectory as well, with a lesser menopause-associated rise in women with obesity compared to women of normal weight. These patterns may have implications for symptoms, because women with obesity are known to have more severe vasomotor symptoms before their FMP, but fewer report severe vasomotor symptoms once they are postmenopausal [21].

The trajectory of the transition itself may also be an important determinant of a woman's menopause journey. Those who have an earlier onset of menstrual cycle changes and enter the MT at relatively younger ages tend to have a longer overall transition, and a more symptomatic one [22]. Of the two well-defined stages of the MT, the early MT is the more variable in terms of duration. Therefore, an early onset of the transition means that a woman will be exposed to the early MT stage for a relatively longer period of time. Such women may need longer periods of treatment. It is known that the duration of vasomotor symptoms is longest for women who have an early onset in their premenopausal or early MT stages or if they appear at a relatively younger age [23].

Symptoms of the MT are worst during the late MT

Longitudinal cohort studies have proven invaluable in assessing how symptoms change across the MT and have allowed for a disentangling of menopause and aging per se. The ability to examine the same participant over many years has also allowed for the ability to detect distinct patterns of change among women to further understand how these short-term patterns may predict longer-term health outcomes or risks.

Vasomotor symptoms peak in prevalence [24], and other 'classic' symptoms of low estrogen appear and/or worsen, such as vaginal dryness and sleep complaints. Depressive symptoms are at their most prevalent during the late MT [25, 26], and risk for major depression is at its highest [26]. Cognitive function, most typically working memory, worsens during the transition, but improves or stabilizes after the FMP and thereafter follows an age-related pattern of change [27]. The relationship of the MT to sleep, apart from its disruption

by vasomotor symptoms, has been debated by some [28], yet sleep remains a very common clinical concern for midlife women [29].

Menopause as an 'accelerant'

For some health issues, menopause causes a temporary change that can be differentiated from change resulting from aging alone, which then reverts back to an age-appropriate curve. Body composition is one example. There is a small overall weight gain associated with the transition of about 2% on average, but lean body mass declines and fat mass increases by >5% [30]. Similar changes are seen with visceral fat mass and carotid intimal medial thickness [31]. After the FMP, visceral fat and carotid intimal medial thickness continue to accrue with age at a rate faster than they did in premenopause, but more slowly than they did during the MT. Low-density lipoprotein cholesterol (LDL-C) increases at almost twice its premenopausal rate during the year before and after the FMP and then returns to its much slower premenopausal rate of increase [32]. Similar changes are seen with arterial stiffness [33]. Bone resorption follows a pattern that is accelerated by the MT as well. Women attain peak bone density in their fourth decade of life. Increased bone loss is not detectable in women undergoing the MT until they reach the late MT, and a period of rapid bone loss, when women lose 5–7% of their skeletal mass, accompanies the period of about 5 years that includes the late transition and the first 1–2 years after the FMP. After this phase of rapid bone loss, bone resorption continues but at a much slower pace [34].

Health parameters that are acutely worsened by the MT may be able to be addressed in clinical practice. Women who begin to develop dyslipidemia early in the MT may benefit from close monitoring and aggressive use of lipid lowering agents and those with worsening endothelial function may be early candidates for initiation of antihypertensive therapy. It is tempting to speculate that antiresorptive treatments directed toward preventing the perimenopausal loss of bone could result in dramatic reduction of subsequent osteoporosis and fracture in older age, but there is as yet no medical evidence to support such practice.

Menopause as a permanent 'resetting'

Perhaps the most dramatic permanent change in physiologic parameters that occurs in concert with the MT is the incidence of metabolic syndrome. Metabolic syndrome is a strong predictor of future cardiovascular disease, type 2 diabetes and dementia; therefore, early detection and prevention is critical to women's health. The prevalence of metabolic syndrome is approximately 10% in women at the time of the FMP, and the incidence rises so rapidly after the transition that >25% of the population has metabolic syndrome by 6 years post FMP [35]. Unfortunately, this relatively rapid rate of accrual of a major cardiometabolic risk factor does not subside. It is particularly important to address metabolic syndrome because it also predicts future risk for Alzheimer disease [36], a major source of morbidity and mortality that disproportionately affects women.

Sleep efficacy decreases with the MT and continues to decline in women. Sleep is being increasingly recognized as an important component of health. Waking after sleep onset is a particularly adverse sleep pattern that has negative implications for long-term cardiovascular morbidity and mortality [37]. Trajectories of poor sleep, assessed by actigraphy from the Study of Women's Health Across the Nation (SWAN), indicate that Black and Hispanic women have worse sleep efficiency and were more likely to follow a sleep trajectory of worsening sleep across the MT [38]. Inadequate sleep is related to cardiometabolic health, and women who sleep less than 5 h per night have approximately twice the risk of developing metabolic syndrome compared to those who do not [29].

Although effective treatment of vasomotor symptoms is associated with improved sleep, other menopause-related changes may influence sleep efficacy for midlife women. Reduced circulating estrogen affects metabolic flexibility by altering adipose tissue function and energy expenditure [39]. Sleep loss, in turn, also has adverse effects on metabolic flexibility, through both neurocognitive and peripheral circadian mechanisms [29]. Understanding the relationship between sleep and health is important for midlife women, as acquiring better sleep habits may also maximize cardiometabolic health.

Long-term implications of the menopause journey

Do MT symptoms predict the future?

There are some associations of menopausal symptoms that seem to predict future risk of disease. Women with prolonged and severe vasomotor symptoms have worse biomarkers of cardiovascular health [40] and have been shown to have an increased risk of CVD events when followed over time [41]. This association requires further testing to clarify the nature of the relationship. It can mean either that a tendency to have severe vasomotor symptoms identifies those at higher CVD risk due to a common, as yet unidentified, pathophysiologic pathway, or that prolonged vasomotor symptoms are somehow causal of CVD. Of course, those who develop clinically detectable metabolic derangements can also be identified as being at excess risk for future CVD and treated accordingly.

Other processes are acutely altered during the MT, and then remit. The increased risk of depressive symptoms and depression and anxiety that accompany the transition do not appear to carry over into later life, and do not necessarily predict future episodes. The acute, rapid phase of bone loss that accompanies the transition does not persist. The menopause-related change in body composition, which can be somewhat attenuated by hormone therapy, does not continue to worsen over time [39]. Thus, while some aspects of the menopause journey do seem to be predictive of future health and disease, others represent a transient disruption. A better understanding of individual factors and vulnerabilities is needed to allow clinicians to tailor their recommendations in a precise manner.

The MT as an adaptive challenge and the role of resilience

In some ways, the MT can be viewed as a disruptive life event that calls upon the organism to adapt. The extent to

which any one individual will be able to adapt will therefore depend upon a number of factors, key among them being genetics and the environment. The timing of menopause is linked to multiple genes and variants [42], and the tempo of the transition is likely related to both genetic (initial follicular endowment) and environmental (influences that may affect the ovarian reserve, such as smoking) factors. A later, shorter transition is associated with fewer vasomotor symptoms and may be overall less disruptive [22, 23]. Individuals reporting more sleep problems report more bothersome vasomotor symptoms [43], as do those who experienced stressful life events [44]. Spirituality may provide protection against symptom severity, as has been observed in a sample of Latter Day Saints [45] and among Hispanic women in the SWAN [46].

When examining health outcomes associated with latent symptom classes in more than 3000 women from the SWAN, those reporting the most physical and mental health symptoms were most likely to develop metabolic syndrome or type 2 diabetes over 20 years of follow-up [47]. Racial and ethnic groups that have historically suffered from discrimination typically report worse and more disruptive symptoms in association with their MT; this is particularly evident among African-American women [23, 38]. Biological vulnerabilities can often be identified and treated medically. However, social determinants of health have long latencies and medicine has a limited ability to treat them – nonetheless, they are important to identify. A socially just approach to menopause requires more than a simple medical inventory and set of prescriptions. Further research is needed to identify and address the social determinants of health that affect a woman's ability to respond to the challenges that the MT imposes for so many.

Conclusions

The menopause journey is inevitable, although current scientific inquiry seeks to eventually make it optional for women. It is not clear that this would be either desirable or beneficial, but the technology is likely to come about. In the meantime, there is much that has been learned about the short-term and long-term symptoms and experience of the MT, as well as its potential health consequences. It can be helpful to conceptualize the MT as an adaptive challenge for women. Those who live a healthy lifestyle and have been blessed with favorable genetics and an environment free of adverse life events may experience minimal disruption, whereas others who are less fortunate and less proactive about their health may struggle for years or decades with bothersome symptoms. It is now clear that the changes in health status that occur during the MT, particularly markers of metabolic health, are important to detect and address, as they may have significant influence on future risk for serious disease. Menopausal symptoms should be treated when they occur, whether with hormones or alternatives, as adequate symptom treatment will improve short-term health and may affect longer-term outcomes. Further advances in genetics, epigenetics and pharmacology should allow clinicians to truly provide precision care for this critical stage of a woman's life.

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References

[1] Hickey M, Hunter MS, Santoro N, et al. Normalising menopause. BMJ. 2022;377:e069369. doi: 10.1136/bmj-2021-069369.
[2] Reddy S. What if we could get rid of menopause? Wall Street Journal. 2023 July 14; 2023 [cited 2024 Jul 20]; Sect. The Saturday Essay. Available from: https://www.wsj.com/articles/what-if-we-could-get-rid-of-menopause-7adbc4e0.
[3] Skinner L, Lawflash RJ. 2023 [Internet]. [cited 2024]. Available from: https://www.morganlewis.com/pubs/2023/01/uk-government-confirms-approach-to-menopause-in-the-workplace#:~:text=Although%20the%20government%20has%20not,menopause%20and%20how%20they%20can.
[4] Jackson LM, Parker RM, Mattison DR, editors. The clinical utility of compounded bioidentical hormone therapy: a review of safety, effectiveness, and Use. Washington (DC): National Academies Press (US); 2020.
[5] Jiang X, Bossert A, Parthasarathy KN, et al. Safety assessment of compounded non-FDA-approved hormonal therapy versus FDA-approved hormonal therapy in treating postmenopausal women. Menopause. 2021;28(8):867–874. doi: 10.1097/GME.0000000000001782.
[6] Harlow SD, Gass M, Hall JE, et al. Executive summary of the Stages of Reproductive Aging Workshop + 10: addressing the unfinished agenda of staging reproductive aging. J Clin Endocrinol Metab. 2012;97(4):1159–1168. doi: 10.1210/jc.2011-3362.
[7] Freeman EW, Sammel MD, Liu L, et al. Hormones and menopausal status as predictors of depression in women in transition to menopause. Arch Gen Psychiatry. 2004;61(1):62–70. doi: 10.1001/archpsyc.61.1.62.
[8] El Khoudary SR, Greendale G, Crawford SL, 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;26(10):1213–1227. doi: 10.1097/GME.0000000000001424.
[9] Robertson DM, Burger HG. Reproductive hormones: ageing and the perimenopause. Acta Obstet Gynecol Scand. 2002;81(7):612–616. doi: 10.1080/j.1600-0412.2002.810706.x.

[10] Mitchell ES, Woods NF. Symptom experiences of midlife women: observations from the Seattle Midlife Women's Health Study. Maturitas. 1996;25(1):1–10. doi: 10.1016/0378-5122(96)01047-x.
[11] Burger HG, Dudley EC, Robertson DM, et al. Hormonal changes in the menopause transition. Recent Prog Horm Res. 2002;57(1):257–275. doi: 10.1210/rp.57.1.257.
[12] Santoro N, Brown JR, Adel T, et al. Characterization of reproductive hormonal dynamics in the perimenopause. J Clin Endocrinol Metab. 1996;81(4):1495–1501. Apr doi: 10.1210/jcem.81.4.8636357.
[13] Hale GE, Robertson DM, Burger HG. The perimenopausal woman: endocrinology and management. J Steroid Biochem Mol Biol. 2014;142:121–131. doi: 10.1016/j.jsbmb.2013.08.015.
[14] Lawley SD, Sammel MD, Santoro N, et al. Mathematical recapitulation of the end stages of human ovarian aging. Sci Adv. 2024;10(2):eadj4490. doi: 10.1126/sciadv.adj4490.
[15] Coslov N, Richardson MK, Woods NF. Symptom experience during the late reproductive stage and the menopausal transition: observations from the Women Living Better survey. Menopause. 2021;28(9):1012–1025. doi: 10.1097/GME.0000000000001805.
[16] Gracia CR, Sammel MD, Freeman EW, et al. Defining menopause status: creation of a new definition to identify the early changes of the menopausal transition. Menopause. 2005;12(2):128–135. doi: 10.1097/00042192-200512020-00005.
[17] Santoro N, Crawford SL, El Khoudary SR, et al. Menstrual cycle hormone changes in women traversing the menopause: study of women's health across the nation. J Clin Endocrinol Metab. 2017;102:2218–2229.
[18] Santoro N, Crawford SL, Lasley WL, et al. Factors related to declining luteal function in women during the menopausal transition. J Clin Endocrinol Metab. 2008;93(5):1711–1721. doi: 10.1210/jc.2007-2165.
[19] Randolph JFJr, Zheng H, Sowers MR, et al. Change in follicle-stimulating hormone and estradiol across the menopausal transition: effect of age at the final menstrual period. J Clin Endocrinol Metab. 2011;96(3):746–754. doi: 10.1210/jc.2010-1746.
[20] Sowers MR, Zheng H, McConnell D, et al. Estradiol rates of change in relation to the final menstrual period in a population-based cohort of women. J Clin Endocrinol Metab. 2008;93(10):3847–3852. doi: 10.1210/jc.2008-1056.
[21] Thurston RC, Sowers MR, Sternfeld B, et al. Gains in body fat and vasomotor symptom reporting over the menopausal transition: the study of women's health across the nation. Am J Epidemiol. 2009;170(6):766–774. doi: 10.1093/aje/kwp203.
[22] Paramsothy P, Harlow SD, Nan B, 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):142–149. doi: 10.1097/GME.0000000000000736.
[23] Avis NE, Crawford SL, Greendale G, et al. Duration of menopausal vasomotor symptoms over the menopause transition. JAMA Intern Med. 2015;175(4):531–539. doi: 10.1001/jamainternmed.2014.8063.
[24] Gold EB, Colvin A, Avis N, et al. Longitudinal analysis of the association between vasomotor symptoms and race/ethnicity across the menopausal transition: study of women's health across the nation. Am J Public Health. 2006;96(7):1226–1235. doi: 10.2105/AJPH.2005.066936.
[25] Bromberger JT, Matthews KA, Schott LL, et al. Depressive symptoms during the menopausal transition: the Study of Women's Health Across the Nation (SWAN). J Affect Disord. 2007;103(1–3):267–272. doi: 10.1016/j.jad.2007.01.034.
[26] Freeman EW. Associations of depression with the transition to menopause. Menopause. 2010;17(4):823–827. doi: 10.1097/gme.0b013e3181db9f8b.
[27] Greendale GA, Karlamangla AS, Maki PM. The menopause transition and cognition. JAMA. 2020;323(15):1495–1496. doi: 10.1001/jama.2020.1757.
[28] Freeman EW, Sammel MD, Gross SA, et al. Poor sleep in relation to natural menopause: a population-based 14-year follow-up of midlife women. Menopause. 2015;22(7):719–726. doi: 10.1097/GME.0000000000000392.
[29] Kravitz HM, Kazlauskaite R, Joffe H. Sleep, health, and metabolism in midlife women and menopause: food for thought. Obstet Gynecol Clin North Am. 2018;45(4):679–694. doi: 10.1016/j.ogc.2018.07.008.
[30] Greendale GA, Sternfeld B, Huang M, et al. Changes in body composition and weight during the menopause transition. JCI Insight. 2019;4(5):e124865. doi: 10.1172/jci.insight.124865.
[31] Samargandy S, Matthews KA, Brooks MM, et al. Abdominal visceral adipose tissue over the menopause transition and carotid atherosclerosis: the SWAN heart study. Menopause. 2021;28(6):626–633. doi: 10.1097/GME.0000000000001755.
[32] Matthews KA, Crawford SL, Chae CU, et al. Are changes in cardiovascular disease risk factors in midlife women due to chronological aging or to the menopausal transition? J Am Coll Cardiol. 2009;54(25):2366–2373. doi: 10.1016/j.jacc.2009.10.009.
[33] Samargandy S, Matthews KA, Brooks MM, et al. Arterial stiffness accelerates within 1 year of the final menstrual period: the SWAN Heart Study. Arterioscler Thromb Vasc Biol. 2020;40(4):1001–1008. doi: 10.1161/ATVBAHA.119.313622.
[34] Greendale GA, Sowers M, Han W, et al. Bone mineral density loss in relation to the final menstrual period in a multiethnic cohort: results from the Study of Women's Health Across the Nation (SWAN). J Bone Miner Res. 2012;27(1):111–118. doi: 10.1002/jbmr.534.
[35] Janssen I, Powell LH, Crawford S, et al. Menopause and the metabolic syndrome: the Study of Women's Health Across the Nation. Arch Intern Med. 2008;168(14):1568–1575. doi: 10.1001/archinte.168.14.1568.
[36] Ezkurdia A, Ramírez MJ, Solas M. Metabolic syndrome as a risk factor for Alzheimer's disease: a focus on insulin resistance. Int J Mol Sci. 2023;24(5):4354. doi: 10.3390/ijms24054354.
[37] Yan B, Yang J, Zhao B, et al. Objective sleep efficiency predicts cardiovascular disease in a community population: the sleep heart health study. J Am Heart Assoc. 2021;10(7):e016201.
[38] Kravitz HM, Janssen I, Bromberger JT, et al. Sleep trajectories before and after the final menstrual period in the Study of Women's Health Across the Nation (SWAN). Curr Sleep Med Rep. 2017;3(3):235–250. doi: 10.1007/s40675-017-0084-1.
[39] Marlatt KL, Pitynski-Miller DR, Gavin KM, et al. Body composition and cardiometabolic health across the menopause transition. Obesity (Silver Spring). 2022;30(1):14–27. doi: 10.1002/oby.23289.
[40] Thurston RC, El Khoudary SR, Tepper PG, et al. Trajectories of vasomotor symptoms and carotid intima media thickness in the study of women's health across the nation. Stroke. 2016;47(1):12–17. doi: 10.1161/STROKEAHA.115.010600.
[41] Thurston RC, Aslanidou Vlachos HE, Derby CA, et al. Menopausal vasomotor symptoms and risk of incident cardiovascular disease events in SWAN. J Am Heart Assoc. 2021;10(3):e017416.
[42] Ruth KS, Day FR, Hussain J, et al. Genetic insights into biological mechanisms governing human ovarian ageing. Nature. 2021;596(7872):393–397. doi: 10.1038/s41586-021-03779-7.
[43] Thurston RC, Bromberger JT, Joffe H, et al. Beyond frequency: who is most bothered by vasomotor symptoms? Menopause. 2008;15(5):841–847. doi: 10.1097/gme.0b013e318168f09b.
[44] Arnot M, Emmott EH, Mace R. The relationship between social support, stressful events, and menopause symptoms. PLoS One. 2021;16(1):e0245444. doi: 10.1371/journal.pone.0245444.
[45] Steffen PR, Soto M. Spirituality and severity of menopausal symptoms in a sample of religious women. J Relig Health. 2011;50(3):721–729. doi: 10.1007/s10943-009-9271-9.
[46] Allshouse AA, Santoro N, Green R, et al. Religiosity and faith in relation to time to metabolic syndrome for Hispanic women in a multiethnic cohort of women-Findings from the Study of Women's Health Across the Nation (SWAN). Maturitas. 2018;112:18–23. doi: 10.1016/j.maturitas.2018.03.008.
[47] Reeves AN, Elliott MR, Brooks MM, et al. Symptom clusters predict risk of metabolic-syndrome and diabetes in midlife: the Study of Women's Health Across the Nation. Ann Epidemiol. 2021;58:48–55. doi: 10.1016/j.annepidem.2021.02.011.