Climacteric

ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/icmt20

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To cite this article: S. Cerdas Pérez (2023) Menopause and diabetes, Climacteric, 26:3, 216-221, DOI: 10.1080/13697137.2023.2184252

To link to this article: https://doi.org/10.1080/13697137.2023.2184252

CLIMACTERIC
2023, VOL. 26, NO. 3, 216–221
https://doi.org/10.1080/13697137.2023.2184252

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REVIEW

Menopause and diabetes

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ABSTRACT

In the last 20 years, the prevalence of type 2 diabetes mellitus (T2DM) has tripled in adults aged 20–79 years, affecting more than 25% of people over 50 years of age and especially women during menopause. After the menopause transition, women gain weight, increasing abdominal fat and decreasing lean body mass, with a significant reduction in energy expenditure. Increased insulin resistance and hyperinsulinism characterize this period, aggravated by an increase in plasma proinflammatory cytokines and free fatty acids, and a state of relative hyperandrogenism. Previous recommendations systematically excluded women with T2DM from menopause hormone therapy (MHT); new evidence confirms that MHT significantly reduces the diagnosis of new-onset T2DM and may be beneficial in terms of glycemic control when used for menopause symptom management in patients with pre-existing T2DM. A comprehensive and individualized approach is considered the first line of management for women during this period, especially in T2DM patients or in women at risk of developing the disease. The objectives of this presentation are to review the etiopathogenic factors involved in the increased incidence of new cases of T2DM during menopause, the impact of menopause on T2DM and the role of MHT.

ARTICLE HISTORY
Received 31 December 2022
Revised 10 February 2023
Accepted 14 February 2023
Published online 4 April 2023

KEYWORDS
Menopause; menopause hormone therapy; type 2 diabetes mellitus; metabolic syndrome

This review was presented as a paper at the 18th IMS World Congress, Lisbon, Portugal in October 2022.

Introduction

Over the past few decades, the topic of 'menopause and diabetes' has been the subject of great controversy, especially in relation to the use of menopause hormone therapy (MHT).

The prevalence of type 2 diabetes mellitus (T2DM) is increasing in western countries, indeed reaching epidemic proportions. The global diabetes prevalence in 20–79 year olds in 2021 was estimated to be 10.5% (536.6 million people), rising to 12.2% (783.2 million) in 2045. The prevalence of the disease increases with age, affecting one in four adults older than 65 years. Other important aspects are that one in two diabetic patients ignore their condition and one in six births come from a mother with gestational diabetes, with numerous consequences for the future generations. In addition, more than 5 million deaths are recorded per year, which represents one death every 6 s. Global diabetes-related health expenditures were estimated at USD 966 billion in 2021 and are projected to reach USD 1054 billion by 2045, which negatively impacts all health systems around the world [1].

Any medical intervention that implies a potential reduction in the incidence of T2DM or in the morbidity and mortality of this disease will be of enormous value. Therefore, it is important to review the existing scientific evidence not only for the etiopathogenesis of metabolic disorders present in middle-aged women, but also for the role of MHT on natural history of these disorders.

Metabolic changes during menopause transition and postmenopause

Numerous medical conditions become more prevalent as women age from the menopausal transition, with a higher incidence of metabolic syndrome, T2DM and cardiovascular risk (CVR). Most of these changes, although not all, are closely related to menopause or to changes that occur during this period of life [2,3]. Surgical menopause has been associated with a higher metabolic syndrome incidence, compared with natural menopause [4].

Various phenotypical and metabolic changes occur during women in mid-life, involving an increase in body weight, with central abdominal predominance, deterioration of insulin secretion and sensitivity, reduction of energy expenditure and a progressive reduction of lean mass [5,6]. Visceral adiposity augments the production of proinflammatory cytokines, increases circulating free fatty acids and promotes the generation of reactive oxygen species, contributing to the development of insulin resistance. Reduced energy expenditure and increased inflammation are early events in the development of ovariectomy-induced obesity [7].

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Menopause is also considered a relative androgen excess state with high androgen bioavailability, due to the decrease of estrogen and sex hormone binging globulin circulation. These factors predispose women to the development of metabolic syndrome, T2DM and increased CVR since the menopause transition [8,9].

These observations were confirmed by the Study of Women's Health Across the Nation (SWAN), a multicenter, multiethnic longitudinal study designed to characterize the physiological and psychosocial changes that occur from the transition to menopause and the effect of age, in a total of 3302 women. Among the relevant findings of this study, they observed significant differences related to the ethnicity of participants, with higher incidence of new cases of metabolic syndrome and T2DM especially in Hispanic women. This cohort concluded that weight gain is mainly related to age, but there appears to be a contribution of menopausal endocrine disturbances in addition to aging per se, in the development of metabolic changes [10].

The key factors influencing weight gain during mid-life have been a matter of debate. Studies have suggested that mid-life weight gain is simply a function of aging and cannot be attributed to hormonal changes of the menopause. Despite the fact that estrogen depletion at menopause may favor central abdominal fat accumulation, several other factors can contribute to these metabolic changes and weight gain [11], including dietary factors, sedentarism [12], parity [13], low level of education, family history of obesity [14] sleep disturbances [15] and use of concomitant medication [16] (Figure 1).

Key message

Metabolic changes occur in women during mid-life related to aging, hormonal changes and concomitant factors.

Risk of developing diabetes during the menopause

Numerous publications, although not all [17], report an increased risk of developing T2DM after menopause. Some of those results are detailed in the following. Multiple studies suggest that impaired glucose metabolism after menopause was not related to decreased estrogen concentration but was the result of aging [18]; however, later analysis of data from the SWAN concluded that lower estradiol concentrations are related to higher risk for T2DM development [19].

Risk for T2DM and reduced lifetime exposure to endogenous estrogens

Numerous studies have associated an increased risk of developing T2DM with reduced lifetime exposure to endogenous estrogens, as occurs in women with primary ovarian insufficiency (POI) or early menopause. The European Prospective Investigation into Cancer (EPIC) InterAct study showed that POI in women younger than 40 years old is associated with a 32% higher risk for T2DM, after following up women prospectively for 11 years [20]. A systematic review and meta-analysis of 13 studies, with 191,762 women in total, demonstrated that women with early menopause or POI present increased risk for T2DM (odds ratio 1.12, 95% confidence interval [CI] 1.01–1.20, $p = 0.02$ and $p = 0.001$; and odds ratio 1.53, 95% CI 1.03–2.27, $p = 0.035$ and $p = 0.001$, respectively) [21].

An observational study with 16,299 women reported the association of early menopause at age <45 years with a 20% higher risk for T2DM [22]. Studies in women with surgical menopause including data from the National Health and Nutrition Examination Survey (NHANES) showed similar results [23].

The analysis of 124,379 postmenopausal women from the Women's Health Initiative (WHI) study showed that women with short reproductive lifetimes (30 years between the age

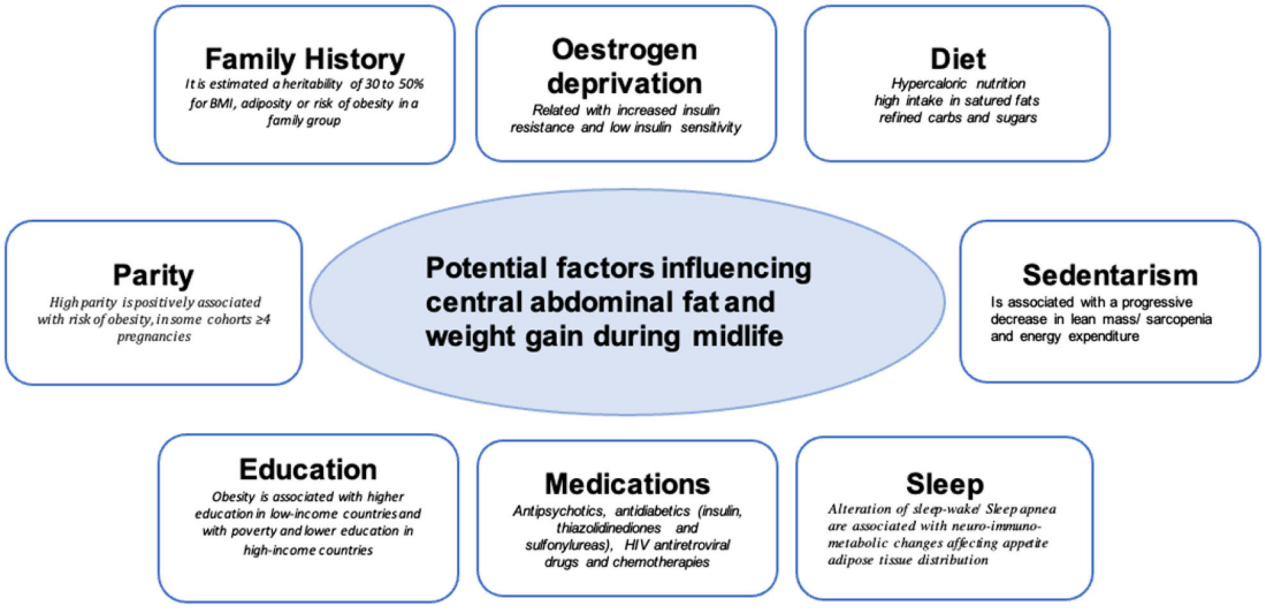

Figure 1. Potential factors influencing central abdominal fat accumulation and weight gain during women's mid-life. BMI, body mass index.

of menarche and the age of the final period) had a 37% greater risk for T2DM compared with those 36–40 years between the age of menarche and the age of the final period [24]. Recently, similar results were reported in a large prospective study of 300,000 middle-aged women from 10 diverse regions in China [25].

Diabetes mellitus and age at menopause

Some cohorts suggested that women with type 1 diabetes mellitus experienced menopause at a younger age [26,27]; but other reports failed to find a significant age difference compared with non-type 1 diabetes mellitus women [28–30], probably in relation to better general health and glucose control than metabolic golds and diabetic complications observed in earlier studies [31]. In T2DM patients, the EPIC study [27] did not find an association of diabetes with age of menopause, contrary to other reports [17,32].

Key message

Risk for T2DM is increased after ovarian function cessation, both in women with natural or surgical menopause as well as in women with POI or early menopause.

Benefits of MHT on glucose homeostasis

Several benefits of MHT on glucose homeostasis and risk for T2DM have been described in different clinical studies. The Heart and Estrogen/Progestin Replacement Study (HERS) [33] found no overall effect of 4.1 years of therapy with estrogen plus progestin for secondary prevention of coronary heart disease in postmenopausal women, despite having observed improvement in glucose control in the MHT arm. Amelioration of other CVR factors was also described in different populations of postmenopausal women (blood pressure, low-density lipoprotein cholesterol, triglycerides, lipoprotein(a), adhesion and coagulation molecules) [34,35]. A reduction in incidence of new cases of T2DM with MHT was reported in different primary prevention studies such as the WHI trials [36], in the observational Nurses' Health Study [37] and in the French Cohort E3N [38].

It is important to note that MHT reduces T2DM incidence independent of the reduction in body weight and waist circumference [39,40].

Vasomotor symptoms have been associated with increased risk of T2DM. In the WHI study, 150.007 women were prospectively examined for the potential association of T2DM with climacteric symptoms. Any vasomotor symptom was associated with an 18% increase in the risk of T2DM (hazard ratio 1.18, 95% CI 1.14–1.22). The more severe the symptoms and the longer their duration, the higher the risk for T2DM [41].

In non-diabetic women, the effect of MHT on the risk to develop T2DM ranges between 20 and 65% and the reduction of A1C was reported around 2.5% [5].

In patients with T2DM, significant reduction of A1C, fasting glucose levels, insulin resistance using euglycemic hyperinsulinemic clamps and other different interventions document reductions of 33% in homeostatic model assessment for insulin resistance [34].

Regarding insulin sensitivity and resistance, the results are non-homogeneous, but most of them showed a favorable trend, probably in relation to the heterogenous methodology of investigation [5] (Figure 2).

Key message

MHT use reduces the risk of new cases of T2DM in non-diabetic postmenopausal women and improves glucose control and several CVR factors in T2DM patients.

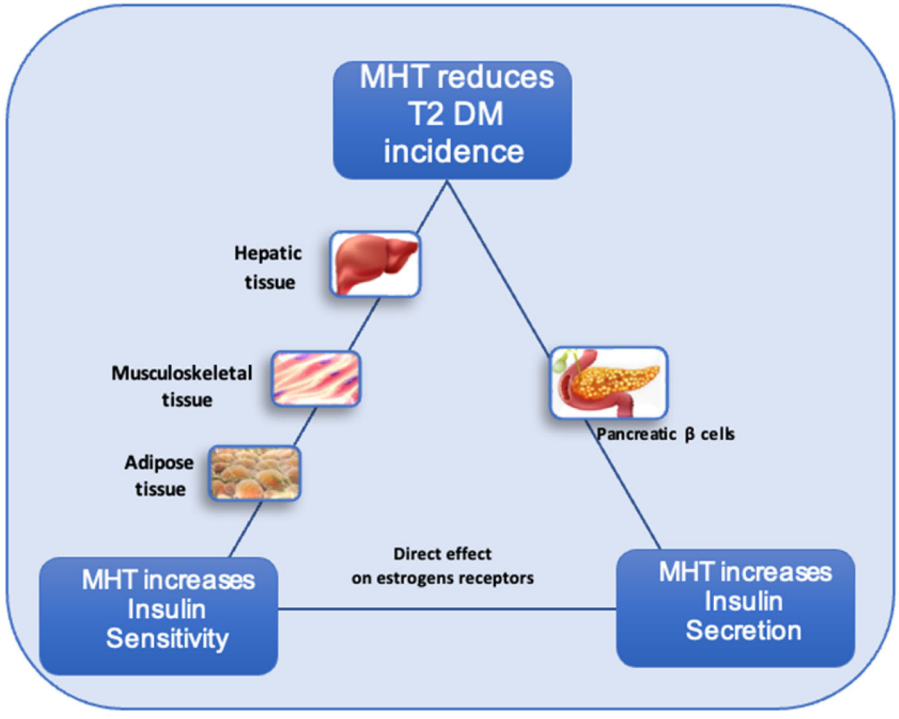

Figure 2. Proposed mechanisms of menopausal hormone therapy (MHT) effect on type 2 diabetes mellitus (T2DM) incidence reduction.

Clinical management of menopausal diabetic women

Previous recommendations systematically excluded women with T2DM from MHT, based on the concept that T2DM is an equivalent of coronary artery disease. Regardless that coronary artery disease is the principal complication of T2DM, not all patients have the same CVR [42].

Major support for the concept that T2DM is an equivalent of cardiovascular disease (CVD) came from Haffner et al.'s study [43]. Subsequent publications confirm that CVD equivalence in diabetics depends on the individual coronary artery status of each patient and on the presence of concomitant risk factors for coronary artery disease [44,45].

Around the world there are currently different positions in relation to the use of MHT as an effective tool in the prevention of chronic diseases [31,46,47], and specifically in the prevention of new cases of T2DM and in the improvement of metabolic glucose control in women with diabetes. Most international societies oppose or do not even mention it [48]. The International Menopause Society (IMS), in the 2016 recommendations document, proposes the use of MHT for management of climacteric syndrome, as a strategy with potential benefits to also improve the CVR risk profile, through its beneficial effects on vascular function, lipid levels and glucose metabolism and the reduction of new-onset diabetes mellitus cases. The IMS notes that consideration of MHT should always be part of an overall strategy including lifestyle recommendations since the menopause transition [49]. Recently, the North American Menopause Society (NAMS) introduces new concepts in relation to this topic, pointing out that MHT significantly reduces the diagnosis of new-onset T2DM (but it is not US government approved for this indication); MHT is not contraindicated in otherwise healthy women with pre-existing T2DM and may be beneficial in terms of glycemic control when used for menopause symptom management [50].

Most of the clinical studies that have evaluated MHT in diabetic patients have done so using conjugated estrogens and medroxyprogesterone acetate, and only a few have evaluated other preparations [5].

The ability to suppress circulating levels of follicle stimulating hormone has been used as a comparative parameter of potency between the different types of estrogens used for MHT, considering the following doses as equipotent: 0.625 mg conjugated estrogens = 1 mg micronized estradiol = 50 μg transdermal estradiol = 5 μg ethinyl estradiol [51].

The metabolic effects of MHT in patients with type 2 diabetes are not only influenced by the type of estrogen but also by the route of administration used. Table 1 presents some of the metabolic differences between the transdermal and oral routes. MHT oral estrogen results in a stronger beneficial metabolic effect, partly explained by the first hepatic metabolism, leading to better suppression of hepatic insulin resistance and hepatic glucose production [5,52]. However, this route is also associated with an increase in triglycerides, coagulation factors and inflammatory marker production, with a potential increase in cardiovascular and thrombotic risks [38,53].

There is now strong evidence to support MHT based on an individualized CVD risk approach in T2DM menopausal women [54]. MHT should not be indicated in women aged >60 years or with >10 years in menopause. For obese T2DM women or those with moderate CVD risk, MHT could be indicated with preference for transdermal 17β-estradiol use. In perimenopause or in T2DM menopausal women aged <60 years or with <10 years in menopause, with low risk for CVD, oral estrogens can be used, as they have the stronger beneficial effects on glucose and lipid metabolism profiles. In patients with a uterus, indication of MHT needs to combine estrogens with progestins with neutral metabolic effect as natural progesterone, norethisterone acetate and dydrogesterone [8].

A comprehensive and individualized approach to women's health is necessary during the transition and postmenopause, in all women, especially in women with T2DM or at risk of developing the disease. Optimizing lifestyle (diet, exercise, smoking cessation, safe levels of alcohol consumption and stress management) and control of CVD factor risks are considered the first line of management [49]. For diabetic patients it is necessary to evaluate and assess comorbidities, and promote weight loss and the appropriate use of pharmacotherapy following the international guidelines. In this general approach, support of positive health behaviors and providing appropriate psychosocial care to the patient and their family members are extremely important [55].

Key message

The menopausal diabetic women approach includes, as a first line of management, optimizing lifestyle and control of metabolic and CVD factor risks. MHT indicated for climacteric syndrome offers several benefits in women with low or moderate CVD risk.

Table 1. Comparative metabolic effects between the administration of transdermal estradiol and oral conjugated estrogens.

Metabolic effect	*Transdermal estradiol*	*Oral conjugated estrogens*
Hepatic tissue delivery	⬇	⬆
Non-hepatic tissue delivery (adipose and muscle tissues)	⬆	⬇
Suppression of hepatic glucose production	⬇	⬆
Plasma glucose reduction	⬇	⬇⬇
Insulin resistance	⬇	⬇⬇
Hepatic synthesis of triglycerides	⬇⬌	⬆
Coagulation factors and inflammatory marker production	⬌	⬆
Plasma LDL and HDL cholesterol ratio	⬇	⬇⬇
New-onset diabetes	⬇	⬇⬇

⬇, lower effect; ⬆, higher effect; ⬌, neutral effect. HDL, high-density lipoprotein; LDL, low-density lipoprotein.

Conclusions

- Aging and decrease in endogenous estrogen concentrations during menopause transition and postmenopause periods are associated with an adverse metabolic profile and an increase in T2DM risk.
- MHT has a favorable effect on glucose homeostasis in women both with and without T2DM, improving glucose homeostasis and reducing the risk of T2DM by enhancing insulin secretion and sensitivity.
- MHT has a favorable effect not only on glucose homeostasis and CVD risk factors, but also on postmenopausal osteoporosis prevention and diabetic bone fragility.
- Women with T2DM would not be systematically excluded from MHT. MHT is indicated in symptomatic T2DM postmenopausal women, after evaluation of their comorbidities and CVD risk stratification.

Potential conflict of interest Nil.

Source of funding Nil.

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References

[1] Sun H, Saeedi P, Karuranga S, et al. IDF diabetes atlas: global, regional and country-level diabetes prevalence estimates for 2021 and projections for 2045. Diabetes Res Clin Pract. 2022;183:109119.
[2] Toth MJ, Tchernof A, Sites CK, et al. Effect of menopausal status on body composition and abdominal fat distribution. Int J Obes. 2000;24(2):226–231.
[3] Tserotas K, Blumel JE. Menopause research in Latin America. Climacteric. 2019;22(1):17–21.
[4] Pu D, Tan R, Yu Q, et al. Metabolic syndrome in menopause and associated factors: a meta-analysis. Climacteric. 2017;20(6):583–591.
[5] Mauvais-Jarvis F, Manson JE, Stevenson JC, et al. Menopausal hormone therapy and type 2 diabetes prevention: evidence, mechanisms, and clinical implications. Endocr Rev. 2017;38(3):173–188.
[6] Lovejoy JC, Champagne CM, de Jonge L, et al. Increased visceral fat and decreased energy expenditure during the menopausal transition. Int J Obes. 2008;32(6):949–958.
[7] Rogers NH, Perfield JW, Strissel KJ, et al. Reduced energy expenditure and increased inflammation are early events in the development of ovariectomy-induced obesity. Endocrinology. 2009;150(5):2161–2168.
[8] Paschou SA, Anagnostis P, Goulis DG, et al. Androgen excess and post-reproductive health. Maturitas. 2018;115:115–116.
[9] Genazzani AR, Monteleone P, Giannini A, et al. Hormone therapy in the postmenopausal years: considering benefits and risks in clinical practice. Hum Reprod Update. 2021;18:1115–1150.
[10] Santoro N, Sutton-Tyrrell K. The SWAN song: study of women's health across the nation's recurring themes. Obstet Gynecol Clin North Am. 2011;38(3):417–423.
[11] Davis SR, Castelo-Branco C, Chedraui P, et al. Writing group of the international menopause society for world menopause day 2012: understanding weight gain at menopause. Climacteric. 2012;15(5):419–429.
[12] Blümel JE, Fica J, Chedraui P, et al. Collaborative group for research of the climacteric in Latin America. Sedentary lifestyle in middle-aged women is associated with severe menopausal symptoms and obesity. Menopause. 2016;23(5):488–493.
[13] Li W, Wang Y, Shen L, et al. Association between parity and obesity patterns in a middle-aged and older Chinese population: a cross-sectional analysis in the Tongji-Dongfeng cohort study. Nutr Metab. 2016;26:13,72.
[14] Bouchard C. Genetics of obesity: What we have learned over decades of research. Obesity. 2021;29(5):802–820.
[15] 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.
[16] Verhaegen AA, Van Gaal LF. Drugs affecting body weight, body fat distribution, and metabolic function-mechanisms and possible therapeutic or preventive measures: an update. Curr Obes Rep. 2021;10(1):1–13.
[17] Monterrosa-Castro A, Blümel JE, Portela-Buelvas K, et al. Collaborative group for research of the climacteric in Latin America (REDLINC). Type II diabetes mellitus and menopause: a multinational study. Climacteric. 2013;16:663–672.
[18] Matthews KA, Gibson CJ, El Khoudary SR, et al. Changes in cardiovascular risk factors by hysterectomy status with and without oophorectomy: study of women's health across the nation. J Am Coll Cardiol. 2013;16:191–200.
[19] Park SK, Harlow SD, Zheng H, et al. Association between changes in oestradiol and follicle-stimulating hormone levels during the menopausal transition and risk of diabetes. Diabet Med. 2017;34(4):531–538.
[20] Brand JS, van der Schouw YT, Onland-Moret NC, et al. The InterAct consortium. age at menopause, reproductive life span, and type 2 diabetes risk: results from the EPIC-InterAct study. Diabetes Care. 2013;36(4):1012–1019.
[21] Anagnostis P, Christou K, Artzouchaltzi AM, et al. Early menopause and premature ovarian insufficiency are associated with increased risk of type 2 diabetes: a systematic review and meta-analysis. Eur J Endocrinol. 2019;1:41–50.
[22] Shen L, Song L, Li H, et al. Association between earlier age at natural menopause and risk of diabetes in middle-aged and older Chinese women: the Dongfeng-Tongji cohort study. Diabetes Metab. 2017;43(4):345–350.
[23] Appiah D, J.Winters JS, Hornung CA. Bilateral oophorectomy and the risk of incident diabetes in postmenopausal women. Diabetes Care. 2014;37(3):725–733.
[24] LeBlanc ES, Kapphahn K, Hedlin H, et al. Reproductive history and risk of type 2 diabetes mellitus in postmenopausal women: findings from the women's health initiative. Menopause. 2017;24(1):64–72.
[25] Wang M, Gan W, Kartsonaki C, et al. Menopausal status, age at natural menopause and risk of diabetes in China: a 10-year prospective study of 300,000 women. Nutr Metab. 2022;19(1):7.
[26] Dorman JS, Steenkiste AR, Foley TP, et al. Menopause in type 1 diabetic women: Is it premature? Diabetes. 2001;50(8):1857–1862.
[27] Brand JS, Onland-Moret NC, Eijkemans MJ, et al. Diabetes and onset of natural menopause: results from the European prospective investigation into cancer and nutrition. Hum Reprod. 2015;30(6):1491–1498.
[28] Yarde F, Van Der Schouw YT, de Valk HW, et al. Age at menopause in women with type 1 diabetes mellitus: the OVADIA study. Hum Reprod. 2015;30:441–446.
[29] Kim C, Cleary PA, Cowie CC, et al. Effect of glycemic treatment and microvascular complications on menopause in women with type 1 diabetes in the diabetes control and complications trial/epidemiology of diabetes interventions and complications (DCCT/EDIC) cohort. Diabetes Care. 2014;37(3):701–708.
[30] Sjöberg L, Pitkäniemi J, Harjutsalo V, et al. Menopause in women with type 1 diabetes. Menopause. 2011;18(2):158–163.
[31] Stuenkel CA. Menopause, hormone therapy and diabetes. Climacteric. 2017;20(1):11–21.
[32] Lopez-Lopez R, Huerta R, Malacara JM. Age at menopause in women with type 2 diabetes mellitus. Menopause. 1999;6:174–178.

[33] Kanaya AM, Herrington D, Vittinghoff E, et al. Glycemic effects of postmenopausal hormone therapy: the heart and Estrogen/progestin replacement study: a randomized, double-blind, placebo-controlled trial. Ann Intern Med. 2003;138(1):1–9.
[34] Salpeter SR, Walsh JM, Ormiston TM, et al. Meta-analysis: effect of hormone-replacement therapy on components of the metabolic syndrome in postmenopausal women. Diabetes Obes Metab. 2006;8(5):538–554.
[35] Anagnostis P, Galanis P, Chatzistergiou V, et al. The effect of hormone replacement therapy and tibolone on lipoprotein(a) concentrations in postmenopausal women: a systematic review and meta-analysis. Maturitas. 2017;99:27–36.
[36] Margolis KL, Bonds DE, Rodabough RJ, et al. Effect of oestrogen plus progestin on the incidence of diabetes in postmenopausal women: results from the women's health initiative hormone trial. Diabetologia. 2004;47(7):1175–1187.
[37] Manson JE, Rimm EB, Colditz GA, et al. A prospective study of postmenopausal estrogen therapy and subsequent incidence of non-insulin-dependent diabetes mellitus. Ann Epidemiol. 1992; 2(5):665–673.
[38] de Lauzon-Guillain B, Fournier A, Fabre A, et al. Menopausal hormone therapy and new-onset diabetes in the French Etude Epidemiologique de Femmes de la Mutuelle Générale de l'Education Nationale (E3N) cohort. Diabetologia. 2009;52(10): 2092–2100.
[39] Duncan AC, Lyall H, Roberts RN, et al. The effect of estradiol and a combined estradiol/progestagen preparation on insulin sensitivity in healthy postmenopausal women. J Clin Endocrinol Metab. 1999;84(7):2402–2407.
[40] Mauvais-Jarvis F. Role of sex steroids in β cell function, growth, and survival. Trends Endocrinol Metab. 2016;27(12):844–855.
[41] Gray KE, Katon JG, LeBlanc ES, et al. Vasomotor symptom characteristics: are they risk factors for incident diabetes? Menopause. 2018;25(5):520–530.
[42] Mosca L, Benjamin EJ, Berra K, et al. Effectiveness-based guidelines for the prevention of cardiovascular disease in women–2011 update: a guideline from the American heart association. Circulation. 2011;123(11):1243–1262.
[43] Haffner SM, Lehto S, Rönnemaa T, et al. Mortality from coronary heart disease in subjects with type 2 diabetes and in nondiabetic subjects with and without prior myocardial infarction. N Engl J Med. 1998;339(4):229–234.
[44] Howard BV, Best LG, Galloway JM, et al. Coronary heart disease risk equivalence in diabetes depends on concomitant risk factors. Diabetes Care. 2006;29(2):391–397.
[45] Bulugahapitiya U, Siyambalapitiya S, Sithole J, et al. Is diabetes a coronary risk equivalent? Systematic review and meta-analysis. Diabet Med. 2009;26(2):142–148.
[46] US Preventive Services Task Force. Hormone therapy for the primary prevention of chronic conditions in postmenopausal persons: US preventive services task force recommendation statement. JAMA. 2022;328:1740–1746.
[47] Langer RD, Simon JA, Pines A, et al. Menopausal hormone therapy for primary prevention: Why the USPSTF is wrong. Climacteric. 2017;20(5):402–413.
[48] Pan M, Pan X, Zhou J, et al. Update on hormone therapy for the management of postmenopausal women. Biosci Trends. 2022; 16(1):46–57.
[49] Baber RJ, Panay N, Fenton A. 2016 IMS recommendations on women's midlife health and menopause hormone therapy. Climacteric. 2016;19(2):109–150.
[50] The 2022 hormone therapy position statement of the North American menopause society. Menopause. 2022;29:767–794.
[51] Mashchak CA, Lobo RA, Dozono-Takano R, et al. Comparison of pharmacodynamic properties of various estrogen formulations. Am J Obstet Gynecol. 1982;144(5):511–518.
[52] Mauvais-Jarvis F, Clegg DJ, Hevener AL. The role of estrogens in control of energy balance and glucose homeostasis. Endocr Rev. 2013;34(3):309–338.
[53] Elkik F, Gompel A, Mercier-Bodard C, et al. Effects of percutaneous estradiol and conjugated estrogens on the level of plasma proteins and triglycerides in postmenopausal women. Am J Obstet Gynecol. 1982;143(8):888–892.
[54] Slopien R, Wender-Ozegowska E, Rogowicz-Frontczak A, et al. Menopause and diabetes: EMAS clinical guide. Maturitas. 2018; 117:6–10.
[55] El Sayed NA, Aleppo G, Aroda VR, et al. Summary of revisions: standards of care in diabetes-2023. Diabetes Care. 2023;46(Suppl 1):S5–S9.