



## Selección de Resúmenes de Menopausia

Semana del 10 al 16 de Octubre de 2018

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**Maturitas. 2018 Nov;117:6-10. doi: 10.1016/j.maturitas.2018.08.009. Epub 2018 Aug 23.**

### **Menopause and diabetes: EMAS clinical guide.**

Slopien R, Wender-Ozegowska E, Rogowicz-Frontczak A, Meczekalski B, Zozulinska-Ziolkiewicz D, et al.

**INTRODUCTION:** Whether menopause increases the risk of type 2 diabetes mellitus (T2DM) independently of ageing has been a matter of debate. Controversy also exists about the benefits and risks of menopausal hormone therapy (MHT) in women with T2DM. **AIMS:** To summarise the evidence on 1) the effect of menopause on metabolic parameters and the risk of T2DM, 2) the effect of T2DM on age at menopause, 3) the effect of MHT on the risk of T2DM, and 4) the management of postmenopausal women with T2DM. **MATERIALS AND METHODS:** Literature review and consensus of experts' opinions. **RESULTS AND CONCLUSION:** Metabolic changes during the menopausal transition include an increase in and the central redistribution of adipose tissue, as well as a decrease in energy expenditure. In addition, there is impairment of insulin secretion and insulin sensitivity and an increase in the risk of T2DM. MHT has a favourable effect on glucose metabolism, both in women with and in women without T2DM, while it may delay the onset of T2DM. MHT in women with T2DM should be administered according to their risk of cardiovascular disease (CVD). In women with T2DM and low CVD risk, oral oestrogens may be preferred, while transdermal 17 $\beta$ -oestradiol is preferred for women with T2DM and coexistent CVD risk factors, such as obesity. In any case, a progestogen with neutral effects on glucose metabolism should be used, such as progesterone, dydrogesterone or transdermal norethisterone. Postmenopausal women with T2DM should be managed primarily with lifestyle intervention, including diet and exercise. Most of them will eventually require pharmacological therapy. The selection of antidiabetic medications should be based on the patient's specific characteristics and comorbidities, as well on the metabolic, cardiovascular and bone effects of the medications.

**Maturitas. 2018 Nov;117:29-33. doi: 10.1016/j.maturitas.2018.08.012. Epub 2018 Aug 31.**

### **Age at natural menopause and mortality: A survival analysis of elderly residents of São Paulo, Brazil.**

Roman Lay AA, do Nascimento CF, de Oliveira Duarte YA, Porto Chiavegatto Filho AD.

**OBJECTIVE:** To conduct a survival analysis according to age at natural menopause (NM) in a representative sample of elderly women from the municipality of São Paulo, Brazil. **STUDY DESIGN:** We analyzed data from the Health, Well-Being and Aging study (SABE), a cohort that started in 2000. Mortality data up to September 2016 were obtained by linkage from the Program for Mortality Information of São Paulo (PRO-AIM). **MAIN OUTCOME MEASURES:** We used Cox regression to analyze all-cause and cause-specific mortality rates for cardiovascular diseases, respiratory diseases and cancer, according to age at menopause, categorized as <40, 41-44, 45-49, 50-54 (reference) and  $\geq 55$ . **RESULTS:** After 16 years of follow-up, there were 444 deaths, of which 199 were from cardiovascular diseases, 73 from respiratory diseases and 65 from cancer. After adjustment for socioeconomic, reproductive and lifestyle factors, having an early menopause (at age 41-44) was associated with an increased risk of all-cause mortality (HR = 1.48, 95% IC: 1.03, 2.14) relative to NM at 50-54 years. Women aged 41-44 and 45-49 at NM had twice the risk of cancer mortality of the reference group. We did not find significant associations between age at NM and cause-specific mortality for respiratory and cardiovascular diseases. **CONCLUSIONS:** Our findings suggest that early menopause is associated with all-cause mortality in the largest city of Latin America. In addition, earlier age at NM was associated with cancer mortality. These results suggest that age at NM may be a biomarker for mortality, irrespective of country of residence.

**Medicine (Baltimore). 2018 Oct;97(41):e12755. doi: 10.1097/MD.00000000000012755.**

### **Bone mineral loss and cognitive impairment: The PRESENT project.**

Kang HG, Park HY, Ryu HU, Suk SH.

Low bone mineral density (BMD) is correlated with Alzheimer's disease and its severity, but the association remains unclear in adults ( $\geq 50$  years) without a history of stroke or dementia. We assessed BMD and cognitive function using

the Mini-Mental Status Examination (MMSE) in 650 stroke- and dementia-free subjects ( $\geq 50$  years) who were recruited for an early health check-up program between January 2009 and December 2010. The mean age was  $62.9 \pm 8.0$  years and mean MMSE score was  $27.6 \pm 3.6$ . A total of 361 subjects had reduced BMD: 197 (30.3%) had osteopenia and 154 (23.6%) had osteoporosis, based on criteria of world health organization. A total of 5.4% of the male subjects had osteoporosis, versus 19.8% of the female subjects. After adjusting for age, sex, education, and other possible confounding factors such as hypertension, diabetes mellitus, and smoking, the estimated odds ratio for cognitive impairment was 1.72 for the osteopenia group (95% confidence interval [CI] 1.09-2.14,  $P = .019$ ) and 2.81 for the osteoporosis group (95% CI 1.78-4.45,  $P < .001$ ). Low BMD is correlated with cognitive impairment in community-dwelling adults aged 50 years and above without any medical history of stroke or dementia, especially in women. A community-based, early life, preventive osteoporosis education campaign might decrease the incidence of dementia.

**Am J Obstet Gynecol. 2018 Oct 9. pii: S0002-9378(18)30871-8. [Epub ahead of print]**

### **Hysterectomy status and all-cause mortality in a 21-year Australian population-based cohort study.**

Wilson LF, Pandeya N, Byles J, Mishra GD.

**BACKGROUND:** Hysterectomy is a common surgical procedure, predominantly performed when women are between 30 and 50 years old. One in three women in Australia has had a hysterectomy by the time they are 60 years old, and 30% have both ovaries removed at the time of surgery. Given this high prevalence, it is important to understand the long-term effects of hysterectomy. In particular, women who have a hysterectomy/oophorectomy at younger ages are likely to be pre- or perimenopausal and may experience greater changes in hormone levels and a shortened reproductive lifespan than women who have a hysterectomy when they are older and postmenopausal. Use of menopausal hormone therapy after surgery may compensate for these hormonal changes. To inform clinical decisions about post-surgery management of women who have a hysterectomy prior to menopause (i.e. average age at menopause 50 years), it is useful to compare women with a hysterectomy to women with no hysterectomy and to stratify the hysterectomy status by whether or not women have had a bilateral oophorectomy, or used menopausal hormone therapy. **OBJECTIVES:** To investigate whether women who had a hysterectomy with ovarian conservation or a hysterectomy and bilateral oophorectomy before the age of 50 years were at a higher risk of premature all-cause mortality compared to women who did not have this surgery before the age of 50. To explore whether use of menopausal hormone therapy modified these associations. **STUDY DESIGN:** Women from the mid-cohort (born 1946-1951) of the Australian Longitudinal Study on Women's Health were included in our study sample ( $n = 13,541$ ). Women who reported a hysterectomy (with and without both ovaries removed) before the age of 50 were considered exposure at risk and compared with women who did not report these surgeries before 50 years. To explore effect modification by use of menopausal hormone therapy we further stratified hysterectomy status by menopausal hormone therapy use. Risk of all-cause mortality was assessed using inverse-probability weighted Cox regression models. **RESULTS:** During a median follow-up of 21.5 years, there were 901 (6.7%) deaths in our study sample. Overall, there was no difference in all-cause mortality between women who reported a hysterectomy with ovarian conservation (hazard ratio 0.86; 95% confidence interval 0.72-1.02) or women who reported a hysterectomy and bilateral oophorectomy (hazard ratio 1.02; 95% confidence interval 0.78-1.34) and women with no hysterectomy. When stratified by menopausal hormone therapy use, women with hysterectomy and ovarian conservation before the age of 50, were not at higher risk of all-cause mortality compared to no hysterectomy, regardless of menopausal hormone therapy use status. In contrast, among non-users of menopausal hormone therapy only, women who reported a hysterectomy-bilateral oophorectomy before the age of 50 were at a higher risk of death compared to women with no hysterectomy (hazard ratio 1.81, 95% confidence interval 1.01-3.25). **CONCLUSIONS:** Hysterectomy with ovarian conservation before the age of 50 did not increase risk of all-cause mortality. Among non-menopausal hormone therapy users only, hysterectomy and bilateral oophorectomy before the age of 50 was associated with a higher risk of death.

**Mol Cell Endocrinol. 2018 Oct 8. pii: S0303-7207(18)30284-3. [Epub ahead of print]**

### **Human versus non-human sex steroid use in hormone replacement therapies part 1: Preclinical data.**

Atwood CS, Ekstein SF.

Prior to 2002, hormone replacement therapy (HRT) was considered to be an important component of postmenopausal healthcare. This was based on a plethora of basic, epidemiological and clinical studies demonstrating the health benefits of supplementation with human sex steroids. However, adverse findings from the Women's Health Initiative (WHI) studies that examined the 2 major forms of HRT in use in the US at that time - Premarin (conjugated equine estrogens; CEE) and Prempro (CEE + medroxyprogesterone acetate; MPA), cast a shadow over the use of any form of HRT. Here we review the biochemical and physiological differences between the non-human WHI study hormones - CEE and MPA, and their respective human counterparts 17 $\beta$ -estradiol (E2) and progesterone (P4). Preclinical data from the last 30 years demonstrate clear differences between human and non-human sex steroids on numerous molecular, physiological and functional parameters in brain, heart and reproductive tissue. In contrast to CEE supplementation, which is not always detrimental although certainly not as optimal as E2 supplementation, MPA is clearly not equivalent to P4, having detrimental effects on cognitive, cardiac and reproductive function. Moreover, unlike P4, MPA is clearly antagonistic of the positive effects of E2 and CEE on tissue function. These data indicate that minor chemical changes to human sex steroids result in physiologically distinct actions that are not optimal for tissue health and functioning.

**Menopause.** 2018 Oct 8. doi: [10.1097/GME.0000000000001246](https://doi.org/10.1097/GME.0000000000001246). [Epub ahead of print]

### **Age at natural menopause and life expectancy with and without type 2 diabetes.**

Asllanaj E, Bano A, Glisic M, Jaspers L, Ikram MA, Laven JSE, Völzke H, Muka T, Franco OH.

**OBJECTIVE:** Effective interventions of future health care require a better understanding of the health risks associated with early onset of menopause and diabetes, but the necessary data are scarce. Little quantitative information is available about the combined association of early menopause and diabetes on life expectancy and the number of years lived with and without diabetes. **METHODS:** We included 3,650 postmenopausal women aged 45+ years from the Rotterdam Study, a prospective population-based cohort study. Age at menopause categories were defined as follows: early ( $\leq 44$  y old), normal (45-54 y old), and late ( $\geq 55$  y old). For life table calculations, we used prevalence, incidence rates, and hazard ratios for three transitions (free of diabetes to diabetes, free of diabetes to death, and diabetes to death) stratifying by age at menopause categories and adjusting for confounders. **RESULTS:** Compared with late menopause, the difference in life expectancy for women who experienced early menopause was -3.5 (95% CI, -6.6 to -0.8) years overall and -4.6 (95% CI, -8.9 to -0.9) years without diabetes. Compared with age at normal menopause, the difference in life expectancy for women who experienced early menopause was -3.1 (95% CI, -5.1 to -1.1) years overall and -3.3 (95% CI, -6.0 to -0.6) years without diabetes. **CONCLUSIONS:** Women who experienced early menopause lived less long and spent fewer years without diabetes than women who experienced normal or late menopause.

**Climacteric.** 2018 Oct 8:1-5. doi: [10.1080/13697137.2018.1504916](https://doi.org/10.1080/13697137.2018.1504916). [Epub ahead of print]

### **The use of estradiol metered-dose transdermal spray in clinical practice.**

Fait T, Fialova A, Pastor Z.

**OBJECTIVE:** The aim of this study was to evaluate the use of novel estradiol metered-dose transdermal spray (EMDTS) in the treatment of acute climacteric syndrome. **METHODS:** A multicenter open-label trial was conducted with a 24-week intervention. EMDTS 1.53 mg was given to symptomatic menopausal women. The Menopause Rating Scale (MRS) was used to assess the climacteric syndrome severity. The Friedman non-parametric test and a post-hoc test with Bonferroni correction were used for statistical evaluation. **RESULTS:** A total of 132 women were enrolled in 20 centers, of whom 123 (93.2%) completed the study. The average age of patients was 53.8 years (37-65 years). The study was discontinued by 6.8% of women. The patients were checked at the beginning of the study, and after 12 and 24 weeks. There was a statistically significant drop ( $p < 0.001$ ) in MRS values both after 12 and 24 weeks of therapy. The average MRS values improved by 66.2% between the first and the third visits. The most significant improvement was manifested in patients with initial moderate climacteric syndrome (70.9%). **CONCLUSION:** This study confirms that application of EMDTS offers a novel treatment option for climacteric symptoms.

**Cancer.** 2018 Oct 8. doi: [10.1002/cncr.31687](https://doi.org/10.1002/cncr.31687). [Epub ahead of print]

## Weight loss and breast cancer incidence in postmenopausal women.

Chlebowski RT, Luo J, Anderson GL, Barrington W, Reding K, Simon MS, Manson JE, Rohan TE, et al.

**BACKGROUND:** Although obesity is an established risk factor for postmenopausal breast cancer, the results of weight loss and breast cancer studies are inconsistent. Therefore, we evaluated associations between weight change and breast cancer risk in postmenopausal women in the Women's Health Initiative Observational Study. **METHODS:** Postmenopausal women ( $n = 61,335$ ) who had no prior breast cancer and a normal mammogram had body weight and height measured and body mass index (BMI) calculated at baseline and year 3. Weight change at year 3 was categorized as stable ( $<5\%$ ), loss ( $\geq 5\%$ ), or gain ( $\geq 5\%$ ) with further assessment of weight loss intentionality by self-report. Multivariable Cox proportional hazard regression models were used to evaluate relationships between weight change and subsequent breast cancer incidence. **RESULTS:** During a mean follow-up of 11.4 years with 3061 incident breast cancers, women with weight loss ( $n = 8175$ ) had a significantly lower risk of breast cancer compared with women whose weight remained stable ( $n = 41,139$ ) (hazard ratio [HR], 0.88; 95% confidence interval [CI], 0.78-0.98;  $P = .02$ ) with no interaction by BMI. Adjustment for mammography did not alter findings (HR, 0.88; 95% CI, 0.78-0.99) with no significant difference by weight loss intentionality. Weight gain ( $\geq 5\%$ ) ( $n = 12,021$ ) was not associated with breast cancer risk (HR, 1.02; 95% CI, 0.93-1.11) but was associated with higher triple-negative breast cancer incidence (HR, 1.54; 95% CI, 1.16-2.05). **CONCLUSIONS:** Postmenopausal women who lose weight have lower breast cancer risk than those with stable weight. These findings suggest that postmenopausal women who lose weight may reduce their breast cancer risk.