



## Selección de Resúmenes de Menopausia

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### **Type of menopause, age of menopause and variations in the risk of incident cardiovascular disease: pooled analysis of individual data from 10 international studies.**

Zhu D1, Chung HF1, Dobson AJ1, Pandeya N1,2, Brunner EJ3, Kuh D4, Greenwood DC5, Hardy R6, et al.  
**STUDY QUESTION:** How does the risk of cardiovascular disease (CVD) vary with type and age of menopause?  
**WHAT IS KNOWN ALREADY:** Earlier age at menopause has been linked to an increased risk of CVD mortality and all-cause mortality, but the extent that this risk of CVD varies by type of menopause and the role of postmenopausal HRT use in reducing this risk is unclear. **STUDY DESIGN, SIZE, DURATION:** Pooled individual-level data of 203,767 postmenopausal women from 10 observational studies that contribute to the International collaboration for a Life course Approach to reproductive health and Chronic disease Events (InterLACE) consortium were included in the analysis. **PARTICIPANTS/MATERIALS, SETTING, METHODS:** Postmenopausal women who had reported menopause (type and age of menopause) and information on non-fatal CVD events were included. Type of menopause (natural menopause and surgical menopause) and age at menopause (categorised as <35, 35-39, 40-44, 45-49, 50-54 and ≥55 years) were exposures of interest. Natural menopause was defined as absence of menstruation over a period of 12 months (no hysterectomy and/or oophorectomy) and surgical menopause as removal of both ovaries. The study outcome was the first non-fatal CVD (defined as either incident coronary heart disease (CHD) or stroke) event ascertained from hospital medical records or self-reported. We used Cox proportional hazards models to estimate hazard ratios (HRs) and 95% CI for non-fatal CVD events associated with natural menopause and surgical menopause. **MAIN RESULTS AND THE ROLE OF CHANCE:** Compared with natural menopause, surgical menopause was associated with over 20% higher risk of CVD (HR 1.22, 95% CI 1.16-1.28). After the stratified analysis by age at menopause, a graded relationship for incident CVD was observed with lower age at menopause in both types of natural and surgical menopause. There was also a significant interaction between type of menopause and age at menopause ( $P < 0.001$ ). Compared with natural menopause at 50-54 years, women with surgical menopause before 35 (2.55, 2.22-2.94) and 35-39 years (1.91, 1.71-2.14) had higher risk of CVD than those with natural menopause (1.59, 1.23-2.05 and 1.51, 1.33-1.72, respectively). Women who experienced surgical menopause at earlier age (<50 years) and took HRT had lower risk of incident CHD than those who were not users of HRT. **LIMITATIONS, REASONS FOR CAUTION:** Self-reported data on type and age of menopause, no information on indication for the surgery (e.g. endometriosis and fibroids) and the exclusion of fatal CVD events may bias our results. **WIDER IMPLICATIONS OF THE FINDINGS:** In clinical practice, women who experienced natural menopause or had surgical menopause at an earlier age need close monitoring and engagement for preventive health measures and early diagnosis of CVD. Our findings also suggested that timing of menopause should be considered as an important factor in risk assessment of CVD for women. The findings on CVD lend some support to the position that elective bilateral oophorectomy (surgical menopause) at hysterectomy for benign diseases should be discouraged based on an increased risk of CVD.

**Eur J Obstet Gynecol Reprod Biol. 2020 Jun 9;252:43-49. [Epub ahead of print]**

### **Women with low quality of life by cervantes-short form scale choose menopausal hormone therapy.**

Laiz MF1, Sánchez AH2, Delgado DV3, Martín PJC4.

**OBJECTIVES:** The aim of the study is to assess whether women who choose to use menopausal hormone therapy (MHT) have lower quality of life (QoL) than those who do not initiate it using Cervantes short form scale (C-SF), and analyze sociodemographic factors associated with lower QoL in women. **STUDY DESIGN:** A cross-sectional descriptive observational study was made in four hundred and eighty women with climacteric symptoms. **RESULTS:** Mean age was 51.1 years. Two hundred and sixty-one women (54.3 %) started MHT. The sample's global mean in C-SF score was  $51.3 \pm 13.9$ . Women who choose to use MHT have higher score in C-SF (lower QoL) than women who reject it ( $58.7 \pm 15.9$  vs  $46.7 \pm 12.8$ ;  $p < 0.001$ ). We found higher score in women with early menopause ( $53.7 \pm 15.9$  vs  $49.7 \pm 13.1$ ;  $p = 0.037$ ); with no obesity (<30 vs >30 BMI) ( $52.8 \pm 13.5$  vs  $41.0 \pm 8.2$ ;  $p = 0.002$ ); with previous malignancies ( $56.2 \pm 18.2$  vs  $50.2 \pm 13.5$ ;  $p = 0.020$ ) and without sexual activity ( $58.0 \pm 25.4$  vs  $50.4 \pm 13.1$ ;  $p = 0.009$ ).

No differences were found in C-SF score with respect to tobacco habits or physical activity. In the multivariate analysis, the variable independently associated to lower QoL by C-SF (high score) was to be a woman who want to initiate MHT ( $p = 0.004$ ). **CONCLUSIONS:** Women who choose to use MHT due to menopausal symptoms have lower quality of life measured by C-SF scale. Women with early menopause, with no obesity ( $<30$  BMI), without sexual activity and with previous malignances have lower quality of life measured by C-SF scale. Women with early menopause have more psychic symptoms like nervousness, fatigue and sleep complaints by C-SF scale than women with natural menopause.

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### **Altered endothelial ETB receptor expression in postmenopausal women.**

Kuczmariski AV1, Shoemaker LN1, Hobson JC1, Edwards DG1, Wenner MM1.

The endothelin system plays an important role in mediating vascular function. The endothelin-B receptor (ETBR) on endothelial cells mediates vasodilation via nitric oxide production. The vasodilatory effect of the ETBR is lost following menopause and may contribute to impaired vascular endothelial function in postmenopausal women (PMW). However, it is unclear if these functional changes are due to changes in ETBR expression on the endothelium. Therefore, the purpose of this study was to test the hypothesis that endothelial cell ETBR expression is lower in PMW compared to young women (YW). Primary endothelial cells were harvested from the antecubital vein of healthy PMW ( $n=15$ ,  $60 \pm 6$  yrs) and YW ( $n=15$ ,  $22 \pm 2$  yrs). Cells were identified as endothelial cells by staining for vascular endothelial cadherin, and nuclear integrity was assessed using 4',6-diamidino-2-phenylindole (DAPI). Within those cells, ETBR was quantified using immunocytochemistry; fluorescence intensity was measured in 30 cells and averaged for each participant. Endothelial function was assessed using brachial artery flow-mediated dilation (FMD). Endothelial cell ETBR expression was lower in PMW ( $0.46 \pm 0.11$  AU) compared to YW ( $0.58 \pm 0.14$  AU;  $P=0.02$ ). Furthermore, significant correlations between ETBR expression and FMD ( $r=0.47$ ,  $P<0.01$ ), total cholesterol ( $r = -0.38$ ,  $P=0.04$ ), and LDL cholesterol ( $r = -0.39$ ,  $P=0.03$ ) were observed. These data demonstrate that endothelial cell ETBR expression is attenuated in PMW. These novel findings provide additional insight into the mechanisms underlying vascular endothelial dysfunction in PMW.

**Climacteric. 2020 Jun 18:1-13. doi: 10.1080/13697137.2020.1767568. [Epub ahead of print]**

### **The impact of menopausal hormone therapy on overall mortality-a comprehensive review.**

Stute P1, Stadler A1, Heufelder A2.

Menopausal hormone therapy (MHT) is indicated for menopausal symptom relief. However, MHT has also been shown to be beneficial for prevention of long-term estrogen deficiency sequelae including mortality. Based on a comprehensive literature review on MHT and mortality, the authors' recommendations are as follows: in postmenopausal women, MHT appears to confer a (significant) reduction in overall mortality; the benefit especially applies to women who initiate long-term MHT early after menopause; in women with prevalent cardiovascular risk factors (except for diabetes mellitus, where results are mixed), the benefit of MHT on overall mortality is even more pronounced; and, however, study results are difficult to compare due to heterogeneous study designs.

**Front Aging Neurosci. 2020 May 29;12:129. doi: 10.3389/fnagi.2020.00129. eCollection 2020.**

### **Fitness Level Influences White Matter Microstructure in Postmenopausal Women.**

Harasym D1,2, Turco CV3, Nicolini C3, Toepp SL3, Jenkins EM3, Gibala MJ3, Noseworthy MD1, Nelson AJ1,3.

Aerobic exercise has both neuroprotective and neurorehabilitative benefits. However, the underlying mechanisms are not fully understood and need to be investigated, especially in postmenopausal women, who are at increased risk of age-related disorders such as Alzheimer's disease and stroke. To advance our understanding of the potential neurological benefits of aerobic exercise in aging women, we examined anatomical and functional responses that may differentiate women of varying cardiorespiratory fitness using neuroimaging and neurophysiology. A total of 35 healthy postmenopausal women were recruited ( $59 \pm 3$  years) and cardiorespiratory fitness estimated ( $22-70$  mL/kg/min). Transcranial magnetic stimulation was used to assess -aminobutyric acid (GABA) and glutamate (Glu) receptor function in the primary motor cortex (M1), and magnetic resonance spectroscopy (MRS) was used to quantify GABA and Glu concentrations in M1. Magnetic resonance imaging was used to assess mean cortical thickness (MCT)

of sensorimotor and frontal regions, while the microstructure of sensorimotor and other white matter tracts was evaluated through diffusion tensor imaging. Regression analysis revealed that higher fitness levels were associated with improved microstructure in pre-motor and sensory tracts, and the hippocampal cingulum. Fitness level was not associated with MCT, MRS, or neurophysiology measures. These data indicate that, in postmenopausal women, higher cardiorespiratory fitness is linked with preserved selective white matter microstructure, particularly in areas that influence sensorimotor control and memory.

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### **An extended Menopause Rating Scale II: a retrospective data analysis.**

Honermann L1, Knabben L1, Weidlinger S1, Bitterlich N2, Stute P1.

**Objective:** This study aims to discuss a statistically reasonable inclusion of additional questions in the Menopause Rating Scale II (MRS II) for daily use in clinical practice. **Methods:** Retrospective data analysis was performed (cantonal ethics committee No. 2016-01179). The MRS II was extended with the parameters 'changes in weight', 'headaches', 'skin changes', 'changes in hair growth', 'hair loss', and whether therapy was desired. Data from 419 women seeking medical advice in our menopause center were collected between April 2009 and April 2017. Cronbach's alpha was used to measure internal consistency of the extended questionnaire. **Results:** For the conventional MRS II (N = 340 of 419, 81.1%), the internal consistency measured with Cronbach's alpha increased from 0.805 to 0.820 considering 'changes in weight' (N = 237, 56.6%), to 0.815 considering 'headaches' (N = 247, 58.9%), and to 0.815 considering 'skin changes' (N = 236, 56.3%) if these additional parameters were added separately. Cronbach's alpha increased from 0.805 to 0.835 (N = 224, 53.5%) if these parameters were added at once. Desire for therapy varied between 42.1% for 'changes in hair growth' (N = 38, 9.1%) and 60.6% for 'hair loss' (N = 33, 7.9%). **Conclusion:** We suggest including the items 'changes in weight', 'headaches', and 'skin changes' in the MRS II as our results show even higher internal consistency with these symptoms and as the wish for therapy was high.

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### **Vitamin D supplementation after the menopause.**

Pérez-López FR1, Chedraui P2, Pilz S3.

The purpose of this review was to assess recent evidence regarding the effects of low vitamin D levels on some highly prevalent clinical conditions of postmenopausal women. We reviewed and selected recent literature regarding menopause-related conditions associated with vitamin D deficiency and interventions to manage them. Low circulating 25-hydroxyvitamin D (25(OH)D) levels related to menopause are linked to diet, lifestyle, changes in body composition, insulin sensitivity, and reduced physical activity. Vitamin D supplementation increases serum 25(OH)D levels while normalizing parathyroid hormone and bone markers, and in women with serum 25(OH)D levels below 10 ng/ml supplementation may improve bone mineral density. Low vitamin D status has been associated with the metabolic syndrome, high triglyceride levels, and low high-density lipoprotein cholesterol levels. When compared with placebo, vitamin D supplementation may lower the risk of the metabolic syndrome, hypertriglyceridemia, and hyperglycemia. There is an inverse relationship between fat mass and serum 25(OH)D levels and, therefore, the dosage of supplementation should be adjusted according to the body mass index. Although vitamin D supplementation may improve glucose metabolism in prediabetic subjects, data regarding muscle strength are conflictive. There is evidence that vitamin D over-treatment, to reach extremely high circulating 25(OH)D levels, does not result in better clinical outcomes. The identification and treatment of vitamin D deficiency in postmenopausal women may improve their general health and health outcomes. Vitamin D supplementation should preferably be based on the use of either cholecalciferol or calcifediol.