



# Menopause

The Journal of The North American Menopause Society

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## Articles

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### **Association between serum estradiol level and coronary artery calcification in postmenopausal women**

Gyun-Ho Jeon, MD, MS, Sung Hoon Kim, MD, PhD, Sung-Cheol Yun, PhD, Hee Dong Chae, MD, PhD, Chung-Hoon Kim, MD, PhD, and Byung Moon Kang, MD, PhD

*This study estimated whether coronary artery calcification is associated with serum estradiol level in postmenopausal women. Retrospective analyses suggest that a higher level of estradiol possibly lowers the calcified-plaque burden of coronary arteries in postmenopausal women.*

908

### **Augmentation of venlafaxine and selective serotonin reuptake inhibitors with zolpidem improves sleep and quality of life in breast cancer patients with hot flashes: a randomized, double-blind, placebo-controlled trial**

Hadine Joffe, MD, MSc, Ann Partridge, MD, MPH, Anita Giobbie-Hurder, MS, Xiaochun Li, PhD, Karleen Habin, RN, MPH, Paul Goss, MD, PhD, Eric Winer, MD, and Judy Garber, MD, MPH

*Augmentation of serotonin-norepinephrine reuptake inhibitors and selective-serotonin reuptake inhibitors with zolpidem improves sleep and quality of life in breast cancer survivors who have sleep disturbance associated with hot flashes. Adding a hypnotic agent to serotonin-norepinephrine reuptake inhibitors/selective-serotonin reuptake inhibitors optimizes hot flash therapy by helping women to sleep through nighttime hot flashes, suggesting that treatments targeting sleep may be an important supplemental strategy to optimize well-being.*

917

### **Longitudinal association of vasomotor symptoms and psychosocial outcomes among postmenopausal women in the United States: a population-based study**

Kristen B. Van Dole, PhD, MSPH, Rachel E. Williams, PhD, MS, Rebekkah S. Brown, DrPH, Bradley Gaynes, MD, MPH, Robert DeVellis, PhD, and Michele Jonsson Funk, PhD

*This study shows a small increase in psychosocial symptoms with increasing vasomotor symptoms and thus provides further evidence of an association between vasomotor symptoms and psychosocial symptoms using a validated instrument in a population-based study.*

924

### **Changes in sexual problems over time in women with and without early-stage breast cancer**

Maria Pérez, MA, Ying Liu, MD, PhD, Mario Schootman, PhD, Rebecca L. Aft, MD, PhD, Kenneth B. Schechtman, PhD, William E. Gillanders, MD, and Donna B. Jeffe, PhD

*This study evaluated whether age-matched women with and without early-stage breast cancer differentially experience sexual problems over time and whether changes in women's problems differ by type of surgical procedure. Results show that patients and controls experienced few sexual problems over time, and in fact, controls were more likely to report sexual problems at subsequent interviews, whereas patients were not.*

938

**Early menopause predicts angina after myocardial infarction**

Susmita Parashar, MD, MPH, MS, Kimberly J. Reid, MS,  
John A. Spertus, MD, MPH, FACC, Leslee J. Shaw, PhD,  
and Viola Vaccarino, MD, PhD

*This study examines whether younger age at menopause increases risk of post-myocardial infarction (MI) angina. Results show that women with early menopause are at higher risk of angina after MI, independent of comorbidities, severity of MI, and quality of care.*

946

**Menopausal symptom experience before and after stopping estrogen therapy in the Women's Health Initiative randomized, placebo-controlled trial**

Robert L. Brunner, PhD, Aaron Aragaki, MS, Vanessa Barnabei, MD, PhD,  
Barbara B. Cochrane, PhD, RN, Margery Gass, MD, Susan Hendrix, DO,  
Dorothy Lane, MD, MPH, Judith Ockene, PhD, Nancy F. Woods, PhD, RN,  
Shagufta Yasmeen, MD, and Marcia Stefanick, PhD

*This study shows that conjugated equine estrogens (CEE) significantly reduced vasomotor symptoms and vaginal dryness in women with baseline symptoms but increased breast tenderness. The likelihood of experiencing symptoms was significantly higher after stopping CEE than placebo regardless of baseline symptom status. These potential effects should be considered before initiating CEE to relieve menopausal symptoms.*

955

**Metabolic syndrome and bone metabolism: the Camargo Cohort Study**

José L. Hernández, PhD, José M. Olmos, PhD, Emilio Pariente, MD,  
Josefina Martínez, PhD, Carmen Valero, PhD, Pilar García-Velasco, MD,  
Daniel Nan, PhD, Javier Llorca, PhD, and Jesús González-Macías, PhD

*This study evaluated bone mineral density, prevalent vertebral and nonvertebral fractures, and calcitropic hormones and bone turnover markers in individuals with and without metabolic syndrome.*

962

**Role of androgens in women's sexual dysfunction**

Rosemary Basson, MD, FRCP(UK), Lori A. Brotto, PhD, A. John Petkau, PhD,  
and Fernand Labrie, MD, PhD

*Androgen metabolites, specifically androsterone glucuronide, reflect intracellular and ovarian sources of testosterone. In this study, it was predicted that women with sexual dysfunction had significantly lowered levels of metabolites. Significantly lower levels of two precursor steroids but not a major androgen metabolite were found in women with hypoactive sexual desire disorder.*

972

**Symptom clusters during the late menopausal transition stage: observations from the Seattle Midlife Women's Health Study**

Lori Cray, PhD, RN, Nancy Fugate Woods, RN, PhD, FAAN,  
and Ellen Sullivan Mitchell, PhD

*The analysis in this study demonstrated that shifting the focus from single symptoms to symptom clusters will facilitate the identification of phenotypic profiles, thus facilitating symptom management strategies that can be tailored to meet the needs of individual women.*

978

**Nitric oxide synthase inhibition attenuates cutaneous vasodilation during postmenopausal hot flash episodes**

Kimberly A. Hubing, MS, Jonathan E. Wingo, PhD, R. Matthew Brothers, PhD,  
Juan Del Coso, PhD, David A. Low, PhD, and Craig G. Crandall, PhD

*The increase in skin blood flow during hot flash episodes is mediated, in part, by nitric oxide-dependent mechanisms.*

983

**Effects of testosterone and estrogen replacement on memory function**

Marika C. Möller, MA, Aniko B. Bartfai, PhD,  
and Angelique Flöter Rådestad, MD, PhD

*In a randomized, double-blind, placebo-controlled design, 50 women with surgically induced menopause received estradiol valerate 2 mg in combination with testosterone undecanoate 40 mg daily or with placebo for 24 weeks. Testosterone addition to estrogen treatment had a negative effect on immediate verbal memory, whereas other memory functions were unaffected.*

990

**Polycystic ovary syndrome and early-onset preeclampsia: reproductive manifestations of increased cardiovascular risk**

Susanne M. Veltman-Verhulst, MD, Bas B. van Rijn, MD, PhD,  
H. Egbertine Westerveld, MD, PhD, Arie Franx, MD, PhD,  
Hein W. Bruinse, MD, PhD, Bart C.J.M. Fauser, MD, PhD,  
and Angelique J. Goverde, MD, PhD

*In this study, the cardiovascular risk of women with a history of early-onset preeclampsia and women with polycystic ovary syndrome was evaluated. It is shown that women with polycystic ovary syndrome and early-onset preeclampsia already show an unfavorable cardiovascular risk profile with high need for lifestyle or medical intervention at a young age.*

997

**Serum lipid profile changes during the menopausal transition in Chinese women: a community-based cohort study**

Jin-Ling Zhou, PhD, Shou-Qing Lin, MD, Ying Shen, MD, Ying Chen, PhD,  
Ying Zhang, MD, and Feng-Ling Chen, MD

*Changes in serum lipid profile related to the stages of the menopausal transition as defined by prospective menstrual pattern are studied. The data suggest that the menopausal transition instead of menopause per se is associated with serum lipid profile in community-based women in China.*

**1004**

**Use of complementary and alternative therapy by women in the first 2 years after diagnosis and treatment of invasive breast cancer**

Susan R. Davis, PhD, MB, BS, Marijana Lijovic, PhD, Pam Fradkin, MB, BS, Jo Bradbury, Maria La China, Max Schwarz, MB, BS, and Robin J. Bell, PhD, MB, BS

*In this article, the patterns of consultation with alternative practitioners, use of complementary and alternative medicine commonly used to alleviate menopausal symptoms, and lifestyle changes made by women in the first 2 years after their diagnosis with invasive breast cancer were documented.*

**1010**

**Determining whether women with osteopenic bone mineral density have low, moderate, or high clinical fracture risk**

Lisa Langsetmo, PhD, Suzanne Morin, MD, Christopher S. Kovacs, MD, Nancy Kreiger, PhD, Robert Josse, MD, Jonathan D. Adachi, MD, Alexandra Papaioannou, MD, David Goltzman, PhD, David A. Hanley, MD, Wojciech P. Olszynski, MD, Jerilynn Prior, MD, Sophie A. Jamal, PhD, and the CaMos Research Group

*This article shows that including risk factors such as general health and height loss can be used to provide a highly effective assessment of fracture risk among women with osteopenic bone mineral density.*

**1017**

**Exercise effects in plantar pressure of postmenopausal women**

Marco A. Monteiro, MSc, Ronaldo E. Gabriel, PhD, Manuel Neves e Castro, MD, Mário F. Sousa, MD, João M. Abrantes, PhD, and Maria H. Moreira, PhD

*The effect of a 12-month moderate-to-vigorous exercise program on plantar pressure among postmenopausal women was investigated. The results of this study provide proof that women who exercise have decreased loading of maximal peak pressures and absolute impulses and, consequently, self-reported pain, soreness, and discomfort in the lower extremity.*

**1026**

**Effect of hormone metabolism genotypes on steroid hormone levels and menopausal symptoms in a prospective population-based cohort of women experiencing the menopausal transition**

Timothy R. Rebbeck, PhD, H. Irene Su, MD, MSCE, Mary D. Sammel, ScD, Hui Lin, MS, Teo V. Tran, BA, Clarisa R. Gracia, MD, MSCE, and Ellen W. Freeman, PhD

*In this study, whether genes involved in the metabolism of steroid hormones are associated with hormone levels or menopausal symptoms was evaluated. Results suggest that genotypes are associated with the occurrence of menopause-related symptoms or the timing of the menopausal transition.*

**1035**

**Synergic effect of phytoestrogens and exercise training on cardiovascular risk profile in exercise-responder postmenopausal women: a pilot study**

Eléonor Riesco, PhD, Mylène Aubertin-Leheudre, PhD, Mathieu L. Maltais, BSc, Mélisa Audet, BSc, and Isabelle J. Dionne, PhD

*This study shows that phytoestrogens combined with exercise compared with exercise alone seem to improve body composition and cardiovascular disease risk profile in women who were exercise responders.*

**1040**

**Synthetic progestins induce growth and metastasis of BT-474 human breast cancer xenografts in nude mice**

Yayun Liang, PhD, Indira Benakanakere, PhD, Cynthia Besch-Williford, DVM, PhD, Ryyan S. Hyder, BS, Mark R. Ellersieck, PhD, and Salman M. Hyder, PhD

*The observations in this article suggest that women who ingest progestins for hormone therapy or oral contraception could be more at risk for developing breast cancer because of proliferation of existing latent tumor cells.*

**1048**

**TNFRSF11A and TNFSF11 are associated with age at menarche and natural menopause in white women**

Yan Lu, PhD, Pengyuan Liu, PhD, Robert R. Recker, MD, Hong-Wen Deng, PhD, and Volodymyr Dvornyk, PhD

*This article reports, for the first time, the possible association of two genes, TNFRSF11A (RANK) and its ligand, TNFSF11 (RANKL), with age at menarche and natural menopause in white women.*

**1055**

**Apigenin blocks induction of vascular endothelial growth factor mRNA and protein in progestin-treated human breast cancer cells**

Benford Mafuvadze, MVSc, Indira Benakanakere, PhD, and Salman M. Hyder, PhD

*This study shows that apigenin blocks progestin-dependent induction of vascular endothelial growth factor mRNA and protein and broadly inhibits the ability of progestins to alter the expression of other components of the angiogenesis pathway, including progesterone receptor and vascular endothelial growth factor receptors, in human breast cancer cells.*

**1064**

**Association between polymorphisms in Wnt signaling pathway genes and bone mineral density in postmenopausal Korean women**

Dong-Yun Lee, MD, Hoon Kim, MD, Seung Yup Ku, MD, PhD, Seok Hyun Kim, MD, PhD, Young Min Choi, MD, PhD, and Jung Gu Kim, MD, PhD

*In this study, the association between single nucleotide polymorphisms in Wnt signal pathway genes and circulating osteoprotegerin, soluble receptor activator of the nuclear factor- $\kappa$ B ligand levels, bone turnover markers, and bone mineral density in postmenopausal Korean women was investigated.*

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## Review Articles

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### Statins and bone health in postmenopausal women: a systematic review of randomized controlled trials

Jirong Yue, MD, Xuemei Zhang, BS, Birong Dong, MD, and Ming Yang, MD

*The primary purpose of this review was to determine whether statins can prevent fractures in postmenopausal women; as the secondary and explanatory factors, bone density and bone biomarker data were also evaluated.*

1080

### Effects of soy isoflavones and genistein on glucose metabolism in perimenopausal and postmenopausal non-Asian women: a meta-analysis of randomized controlled trials

Elena Ricci, PhD, Sonia Cipriani, ScD, Francesca Chiaffarino, ScD, Matteo Malvezzi, ScD, and Fabio Parazzini, MD

*In this meta-analysis of randomized controlled trials, isoflavone use was not associated with a significant glycemia reduction in perimenopausal and postmenopausal non-Asian women. However, insulin and homeostasis model assessment insulin resistance changes suggested that soy isoflavones and genistein alone had a beneficial effect on glucose metabolism.*

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## Letters to the Editor

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## Erratum

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