



## Selección de Resúmenes de Menopausia

Semana del 3 al 9 de noviembre de 2021

María Soledad Vallejo. Clínica Quilín. Universidad de Chile

**Mayo Clin Proc. 2021 Nov 1;S0025-6196(21)00634-0. doi: 10.1016/j.mayocp.2021.08.009. Online ahead of print.**  
**The Renin- -Aldosterone System in Postmenopausal Women: The Promise of Hormone Therapy** -20

Felice L Gersh 1, James H O'Keefe 2, Carl J Lavie 3, Brandon M Henry 4

Estradiol (E2) plays an underrecognized role in modulating body-wide systems, including important interactions with the renin-angiotensin-aldosterone system (RAAS). The RAAS is an immunomodulating system that is critical for maintaining homeostasis across multiple organ systems. The diverse interactions between E2 and the RAAS help maintain cardiometabolic homeostasis, including successful physiologic responses to trauma and infectious pathogens. Estradiol deficiency (ie, menopause) results in impaired responses and increased susceptibility to infectious pathogens. Both immune and cardiometabolic function decline with reduced E2 production, in part because the RAAS becomes dysregulated by E2 deficiency, leaving RAAS predominantly in its proinflammatory state and predisposing to systemic low-grade inflammation. Estradiol deficiency and RAAS dysregulation contribute to impaired immune responses and increased incidence of cardiac hypertrophy, hypertension, atherosclerotic cardiovascular disease, arrhythmias, and heart failure. The RAAS consists of dual, counterbalancing pathways-proinflammatory and anti-inflammatory. Estradiol is a signaling agent that plays a major role in determining which RAAS pathway predominates. The proinflammatory pathway is activated early in response to infection or trauma, followed by up-regulation of the anti-inflammatory pathway, to resolve inflammation and to restore homeostasis. Estradiol influences activation of the "switch" to restore the anti-inflammatory state. The dysregulated RAAS is a primary target of current cardiovascular therapeutics focused on blocking portions of its proinflammatory pathway. However, RAAS-modifying pharmaceuticals often provide imperfect solutions to these physiologic disruptions and underscore the need for improved approaches to menopausal medicine. Estradiol therapy and optimal lifestyle practices combined with RAAS-modifying pharmaceuticals may be an ideal strategy to optimize postmenopausal health.

**Maturitas. 2021 Dec;154:25-30. doi: 10.1016/j.maturitas.2021.09.004. Epub 2021 Sep 11.**

### **Impact of menopause on women with systemic lupus erythematosus**

Carrie A Karvonen-Gutierrez 1, Aleda Leis 2

Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by chronic and systemic inflammation affecting multiple organ systems, including an increased risk of cardiovascular disease due to the SLE-associated hyperinflammatory state. SLE shows a strong female predominance, suggesting a potential role of sex hormones in the pathogenesis of the disease. Evidence suggests an earlier age of menopause among women with SLE, despite mixed findings regarding other markers of ovarian aging. In healthy populations, the menopausal transition is associated with important physiologic changes resulting in increased cardiometabolic risk and risk of osteoporosis. Thus, women with SLE who experience the inflammatory effects of the autoimmune condition combined with the (potentially earlier) menopausal transition may represent a particularly vulnerable group of individuals during a particular window of time. Little is known, however, about strategies for cardiovascular risk or bone loss mitigation in women with SLE during the menopausal transition. Further, despite lack of knowledge regarding the burden of menopausal symptoms in women with SLE, existing recommendations provide only cautionary guidance for the use of hormone replacement therapy to address menopausal symptoms in this population. Importantly, the data regarding both SLE and menopause-associated cardiovascular and osteoporotic risk demonstrate the critical need for additional research to identify the type and timing of treatments or interventions needed to best mitigate this increased risk.

**Maturitas. 2021 Dec;154:20-24. doi: 10.1016/j.maturitas.2021.09.003. Epub 2021 Sep 6.**

### **Climacteric symptoms more severe in 2010 than in 2000 - experience of Finnish women aged 52-56 years not now or previously on menopausal hormone therapy**

Maija Lipasti 1, Jaana Jalava-Broman 2, Lauri Sillanmäki 3, Juha Mäkinen 4, Päivi Rautava 5

**Objectives:** To analyze and compare the experience of climacteric symptoms and their associations with sociodemographic and health-related characteristics in two cohorts of Finnish women aged 52-56 years, born ten years apart and not now or previously on menopausal hormone therapy (MHT). **Study design:** Nationwide population-based time-trend study with a large number of participants (n = 1986 + 1988). **Main outcome measures:** The experience of climacteric symptoms was assessed by 12 commonly used menopause-related symptoms. **Results:** Women aged 52-56 experienced more moderate or severe symptoms and fewer mild symptoms in 2010 than in 2000. Being unemployed or inactive was associated with more severe symptoms (P = 0.007), but employment status had no effect on the relative odds estimates. **Conclusions:** The influence of the birth cohort and time-period effects as well as work-related factors on the experience of climacteric symptoms in women not now or previously on MHT needs further research, particularly since the change in the experience of symptoms found in this study occurred within only ten years.

**Biomed Res Int. 2021 Oct 25;2021:7702863. doi: 10.1155/2021/7702863. eCollection 2021.**

### **Possible Risk of Thrombotic Events following Oxford-AstraZeneca COVID-19 Vaccination in Women Receiving Estrogen**

Ava Soltani Hekmat 1, Kazem Javanmardi 1

People who receive the ChAdOx1 nCoV-19 vaccine, particularly perimenopausal women who are on birth control or postmenopausal women who take estrogen supplements, may experience thrombosis and thrombocytopenia. Estrogen and the ChAdOx1 nCoV-19 vaccine both have the potential to cause thrombus in different ways. Some postmenopausal women who are also taking estrogens may develop thrombosis and thrombocytopenia after receiving the ChAdOx1 nCoV-19 vaccine. Therefore, women are encouraged to stop taking drugs containing estrogen before receiving this vaccine. Furthermore, consuming fish oil can help reduce the risk of developing blood clots among women who are in the luteal phase and, thus, have high estrogen levels. In addition, ChAdOx1 nCoV-19's side effects in young women could be mitigated by administering it during the follicular phase.

**Diabetes Care. 2021 Nov 3;dc211565. doi: 10.2337/dc21-1565. Online ahead of print.**

### **Body Fat Distribution, Cardiometabolic Traits, and Risk of Major Lower-Extremity Arterial Disease in Postmenopausal Women**

Guo-Chong Chen 1 2, Rhonda Arthur 2, Victor Kamensky 2, Jin Choul Chai 2, Bing Yu 3, et al.

**Objective:** To assess the relationship between body fat distribution and incident lower-extremity arterial disease (LEAD). **Research design and methods:** We included 155,925 postmenopausal women with anthropometric measures from the Women's Health Initiative who had no known LEAD at recruitment. A subset of 10,894 participants had body composition data quantified by DXA. Incident cases of symptomatic LEAD were ascertained and adjudicated through medical record review. **Results:** We identified 1,152 incident cases of LEAD during a median 18.8 years follow-up. After multivariable adjustment and mutual adjustment, waist and hip circumferences were positively and inversely associated with risk of LEAD, respectively (both P-trend < 0.0001). In a subset (n = 22,561) where various cardiometabolic biomarkers were quantified, a similar positive association of waist circumference with risk of LEAD was eliminated after adjustment for diabetes and HOMA of insulin resistance (P-trend = 0.89), whereas hip circumference remained inversely associated with the risk after adjustment for major cardiometabolic traits (P-trend = 0.0031). In the DXA subset, higher trunk fat (P-trend = 0.0081) and higher leg fat (P-trend < 0.0001) were associated with higher and lower risk of LEAD, respectively. Further adjustment for diabetes, dyslipidemia, and blood pressure diminished the association for trunk fat (P-trend = 0.49), yet the inverse association for leg fat persisted (P-trend = 0.0082). **Conclusions:** Among U.S. postmenopausal women, a positive association of upper-body fat with risk of LEAD appeared to be attributable to traditional risk factors, especially insulin resistance. Lower-body fat was inversely associated with risk of LEAD beyond known risk factors.

**BMC Musculoskelet Disord. 2021 Nov 3;22(1):926. doi: 10.1186/s12891-021-04776-7.**

### **Pregnancy- and lactation-associated osteoporosis with vertebral fractures: a systematic review**

Ying Qian 1, Lei Wang 2, Lili Yu 3, Weimin Huang 4

**Background:** To review, analyze and characterize the pregnancy and lactation-related osteoporosis (PLO) with vertebral fractures based on the extraction data in the previous studies. **Methods:** A comprehensive literature search of

electronic databases including the PubMed, Embase and Web of Science was conducted from January 1st, 1990 to December 1st, 2020. The enrolled data were pooled to analyze the baseline characteristics, clinical features, risk factors and treatment options. Results: A total of 65 articles with 338 cases were enrolled for data extraction. The enrolled cases aged from 19 to 47 years, with a mean value of 35.7 years old. The average body mass index (BMI) was 22.2 kg/m<sup>2</sup> ranged from 16.0 to 39.0 kg/m<sup>2</sup>. Of the 173 cases, 149 cases with vertebral fractures occurred in the first pregnancy, 19 cases in the second pregnancy, four cases in the third pregnancy and one case in the fourth pregnancy. Up to 91.5% of the back pain occurred within the last 3 months of pregnancy and the first 3 months after delivery. The most involved vertebral levels were L2, L1 and T12 accounting for 32.6% of all the fractures. The average fracture numbers were 4.4 levels per patient. The lumbar Z-scores were mostly recorded with a mean value of - 3.2 ranged from - 7.8 to 0. Conclusions: PLO with vertebral fractures is a rare clinical entity, which is more likely to occur in older and thinner pregnant women. Back pain is the clinical complaint and mostly occurs in the late pregnancy and early lactation periods. Most vertebral fractures appear in the first pregnancy but it can occur in any time of pregnancy. Thoracolumbar region is the mostly involved region. As compared with postmenopausal osteoporotic fractures, PLO usually has multiple levels fractures. Bisphosphonates are the most widely used treatment so far, however, many factors need to be taken into account to decide which drug to choose in PLO and further studies are necessary for clear recommendation in the future.

**Eur J Clin Nutr. 2021 Nov 2. doi: 10.1038/s41430-021-01039-5. Online ahead of print.**

### **Dietary inflammatory index and breast cancer risk: an updated meta-analysis of observational studies**

Zahra Hayati 1 2, Mohammad Asghari Jafarabadi 3 4, Saeed Pirouzpanah 5 6

This updated meta-analysis sought to determine whether the pro-inflammatory potential of diet is a risk factor for breast cancer (BrCa) development, for the first time focusing on the effects of design heterogeneity. The search was performed using Scopus, PubMed, and Embase databases. Data were extracted from twenty-one eligible studies, including eleven cohorts (336,085 participants/20,033 incidence cases), and ten case-control studies (9,833 cases/12,752 controls). The random-effect was used to calculate the relative risk (RR) using STATA 16 software. The highest dietary inflammatory index (DII) vs. the lowest category showed 16% increased risk of BrCa (95% CI: 1.06-1.26; I<sup>2</sup> = 62.8%, P (I<sup>2</sup>) < 0.001). This was notable in post-menopausal status (RR = 1.13, 95% CI: 1.04-1.22), women with body mass index (BMI) ≥ 30 kg/m<sup>2</sup> (RR = 1.35, 95% CI: 1.07-1.63), and study populations from developing countries (RR = 1.79, 95% CI: 1.12-2.47). Methodological covariates were subject to subgroup meta-analyses and showed stronger results among case-control studies (RR = 1.50, 95% CI: 1.20-1.80), studies considered age-matched controls (RR = 1.56, 95% CI: 1.19-1.93) and hospital-based controls (RR = 2.11, 95% CI: 1.58-2.64), and cohort studies identified by prolong follow-up durations (RR = 1.13, 95% CI: 1.03-1.22). This updated meta-analysis highlighted the pro-inflammatory diet as a risk factor for BrCa, especially among women in post-menopausal status, obese groups, and developing countries. Meta-analysis in methodological subgroups could improve results, less affected by heterogeneity, and suggested subclassification with important implications for future epidemiological designs and even clinical management.

**Climacteric. 2021 Nov 2;1-6. doi: 10.1080/13697137.2021.1978424. Online ahead of print.**

### **Impact of Global Consensus Statement on compliance with hormonal therapy for surgical menopause**

K Techatraisak 1, M Rattanachaiyanont 1, P Tanmahasamut 1, S Indhavivadhana 1, T Wongwananuruk 1, P Jirakittidul

Objective: Initiation of and compliance with menopausal hormonal therapy (MHT) have been dropping due to the 2002 Women's Health Initiative (WHI) publication. We evaluated the change in practice of MHT for surgical menopause after implementing the 2013 'Global Consensus Statement on MHT' to our institutional guideline. Methods: A retrospective study was conducted in surgically menopausal women newly registering at the Siriraj Menopause Clinic in a university hospital, Thailand, from 1995 to 2013. The patients were categorized into four groups according to periods of MHT initiation: 1995-1998 (control), 2000-2003 (WHI affected), 2005-2008 (post WHI) and 2010-2013 (Global Consensus Statement affected). Their 3-year compliance with MHT was compared using forward stepwise regression analysis. Results: There were 288, 156, 107 and 104 cases in the 1995-1998, 2000-2003, 2005-2008 and 2010-2013 groups. Their mean age at surgery was 42.8 ± 4.7 years. After the first, second and third years, overall compliance was 82.4%, 70.9% and 61.2%, respectively. The 3-year compliance drastically dropped in the 2000-2003

group, and then improved to control level in the 2010-2013 group (51.9% vs. 77.9%,  $p = 0.035$ ). Conclusion: The initiation of MHT continuously dropped during 2000-2013; however, compliance with MHT initiated during 2010-2013 improved after implementing the 2013 'Global Consensus Statement on MHT' to our institutional guideline. Each institute should have a strategy to encourage the initiation of and compliance with MHT for surgical menopause to achieve long-term health benefits.

**Crit Rev Food Sci Nutr. 2021 Nov 1;1-17. doi: 10.1080/10408398.2021.1996330. Online ahead of print.**

## **The influence of vegetarian and vegan diets on the state of bone mineral density in humans**

Alexey Galchenko 1 2, K Gapparova 1, E Sidorova 3

There are so many literatures about vegetarians being less prone to chronic, noninfectious diseases, which are, however, the main cause of the decline in quality of life and mortality in developed countries. However, according to various scientific sources, vegetarian and especially vegan diets often contain less saturated fats, protein, calcium, vitamins D and B12, or long-chain  $\omega$ -3 PUFAs. One of the most common pathology associated with a predominantly plant diet is osteopenia and osteoporosis. An analysis of 13 studies has shown that vegetarians and vegans are at a higher risk of reducing of bone mineral density, thereby increasing the incidence of fractures. the same time, plant-based diets are usually richer in many other micronutrients important for bone health: vitamins C and K, carotenoids, potassium, magnesium, manganese, copper, or silicon. Moreover, with the deepening of our knowledge about the role of nutrients in the body and the features of the nutritional status of the population, the quality of vegetarian and vegan diets also increases. They are less and less prone to micronutrient deficiencies. Recent studies show that BMD, as well as the risk of osteoporotic fractures, at least in vegetarians, equaled these indicators in omnivores.

**Lancet Healthy Longev. 2021 Sep;2(9):e580-e592. doi: 10.1016/S2666-7568(21)00172-0.**

## **Global, regional, and national burden of bone fractures in 204 countries and territories, 1990-2019: a systematic analysis from the Global Burden of Disease Study 2019**

GBD 2019 Fracture Collaborators

Background: Bone fractures are a global public health issue; however, to date, no comprehensive study of their incidence and burden has been done. We aimed to measure the global, regional, and national incidence, prevalence, and years lived with disability (YLDs) of fractures from 1990 to 2019. Methods: Using the framework of the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2019, we compared numbers and age-standardised rates of global incidence, prevalence, and YLDs of fractures across the 21 GBD regions and 204 countries and territories, by age, sex, and year, from 1990 to 2019. We report estimates with 95% uncertainty intervals (UIs). Findings: Globally, in 2019, there were 178 million (95% UI 162-196) new fractures (an increase of 33.4% [30.1-37.0] since 1990), 455 million (428-484) prevalent cases of acute or long-term symptoms of a fracture (an increase of 70.1% [67.5-72.5] since 1990), and 25.8 million (17.8-35.8) YLDs (an increase of 65.3% [62.4-68.0] since 1990). The age-standardised rates of fractures in 2019 were 2296.2 incident cases (2091.1-2529.5) per 100 000 population (a decrease of 9.6% [8.1-11.1] since 1990), 5614.3 prevalent cases (5286.1-5977.5) per 100 000 population (a decrease of 6.7% [5.7-7.6] since 1990), and 319.0 YLDs (220.1-442.5) per 100 000 population (a decrease of 8.4% [7.2-9.5] since 1990). Lower leg fractures of the patella, tibia or fibula, or ankle were the most common and burdensome fracture in 2019, with an age-standardised incidence rate of 419.9 cases (345.8-512.0) per 100 000 population and an age-standardised rate of YLDs of 190.4 (125.0-276.9) per 100 000 population. In 2019, age-specific rates of fracture incidence were highest in the oldest age groups, with, for instance, 15 381.5 incident cases (11 245.3-20 651.9) per 100 000 population in those aged 95 years and older. Interpretation: The global age-standardised rates of incidence, prevalence, and YLDs for fractures decreased slightly from 1990 to 2019, but the absolute counts increased substantially. Older people have a particularly high risk of fractures, and more widespread injury-prevention efforts and access to screening and treatment of osteoporosis for older individuals should help to reduce the overall burden.

**Front Nutr. 2021 Oct 13;8:747877. doi: 10.3389/fnut.2021.747877. eCollection 2021.**

## **Bone and Lean Mass Loss and Cognitive Impairment for Healthy Elder Adults: Analysis of the Nutrition and Health Survey in Taiwan 2013-2016 and a Validation Study With Structural Equation Modeling**

Sheng-Feng Lin 1 2 3, Yen-Chun Fan 1, Wen-Harn Pan 4, Chyi-Huey Bai 1 5 6

**Purpose:** Bone and lean mass loss and cognitive impairment are prevalent in elder adults and have been hypothesized to share a potential link. **Methods:** This nationwide cross-sectional study systemically sampled elder adults aged  $\geq 65$  years and conducted the door-to-door survey. The causal diagrams help to decide which covariates were included in the generalized linear mixed models (GLMMs). The structural equation modeling (SEM) was performed for the validation. **Results:** A total of 535 participants were enrolled and categorized into the normal (67.3%), mild cognitive impairment (18.3%), and dementia groups (14.4%). With increasing in the severity of cognitive impairment, the bone marrow density and lean mass consistently showed the trend of decreasing values. In the GLMMs, a significant association existed between the decrease of the bone mineral density (BMD) and the Mini-Mental State Examination (MMSE) ( $\beta = 5.819$  scores per  $\text{g}/\text{cm}^2$  decrease,  $p = 0.0305$ ) with adjustment of the age, sex, and physical activity. The SEM models confirmed that the MMSE was significantly and directly predicted by the age ( $\beta = 0.1363$ ,  $p = 0.0003$ ) and BMD ( $\beta = 0.1251$ ,  $p = 0.0006$ ) independently and indirectly predicted by lean mass ( $\beta = 0.1138$ ,  $p = 0.0003$ ) through the bone density path. **Conclusion:** In conclusion, an independent association between bone loss and cognitive impairment was existed rather than the confounding effect and the decrease of lean mass indirectly contributed to cognitive impairment by influencing the bone density.

**J Family Reprod Health. 2021 Sep;15(3):150-159. doi: 10.18502/jfrh.v15i3.7132.**

## **Estradiol and COVID-19: Does 17-Estradiol Have an Immune-Protective Function in Women Against Coronavirus?**

Farideh Zafari Zangeneh 1, Maryam Sarmast Shoushtari 2

**Objective:** Female sex hormones have a pro-inflammatory effect, which may help to minimize inflammation. Estrogen's immunoregulatory properties play a significant role in the bi-directional neuroendocrine-immune activity in females. As a result, sex hormones can play a role in men's high mortality rate from coronavirus-2019 (COVID-19). It is aimed to clarify the role of 17-estradiol (E2) in the battle against COVID-19. **Materials and methods:** Until April 2021, a study on PubMed was performed. COVID-19, 17-estradiol (E2), immunoregulatory properties, pregnancy, menopausal symptoms, hormonal therapy, ER/ expression on immune cells, and mortality were some of the concepts used in the search. **Results:** Regulation of pro-inflammatory immune processes against COVID-19 appears to be associated with increased immune function (pro-inflammatory), anti-inflammatory regulation, and antiviral defense. Women with a severe coronavirus infection had higher serum IgG antibody levels than men, and their IgG production was faster in the early stages of infection. 17-estradiol (E2) levels of blood will increase by 100-fold during pregnancy. COVID-19 in pregnant women had a 15-fold lower mortality rate than other women. While menopause replacement therapy (MRT) for pre/post-menopausal women and its effectiveness in reducing COVID-19 infection is debatable. **Conclusion:** MRT may be considered as a viable treatment option for pre/post-menopause women with coronavirus, referring to the fact that sex hormones reduce inflammatory responses and modulate ACE2 expression. The task's difficulty and achieving the desired outcome seem to be challenging.

}