



## Selección de Resúmenes de Menopausia

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### Dry eye disease symptoms and quality of life in perimenopausal and postmenopausal women

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**Objective:** This study aimed to evaluate dry eye disease (DED) symptoms and quality of life (QoL) in a group of perimenopausal and postmenopausal women, based on the Ocular Surface Disease Index (OSDI) questionnaire. **Methods:** An observational study was performed in a group of 1947 perimenopausal and postmenopausal women, aged between 45 and 79 years. The personal data collected were age, menopause status, age at menopause, and OSDI score. **Results:** The mean age of the group was  $54.18 \pm 6.84$  years, with a mean age at menopause of  $49.45 \pm 4.02$  years. The average OSDI score was  $29.20 \pm 19.4$ . The overall prevalence of DED symptoms was 79%, increasing significantly in postmenopausal women, 76.4% vs. 80.5% ( $p = 0.029$ ). In our group, 37.7% had severe DED symptoms. Ocular symptoms, vision-related functions, and environmental trigger scores were higher in postmenopausal women, leading to a lower QoL. The severity of OSDI score increases with age ( $\beta$  coefficient: 0.15 [95% confidence interval: 0.02; -0.28]), while the severity of OSDI score decreases with a later onset age of menopause ( $\beta$  coefficient: -0.27 [95% confidence interval: -0.55; -0.01]). **Conclusions:** DED symptoms are highly prevalent in perimenopausal and postmenopausal women. Postmenopausal women had a higher prevalence of symptoms and higher OSDI scores than perimenopausal women. The severity of DED symptoms and vision-related functions leads to poorer QoL.

**J Allergy Clin Immunol. 2020 Dec 3;S0091-6749(20)31697-3.doi: 10.1016/j.jaci.2020.11.024. Online ahead of print.**

### Hormone Replacement Therapy and Asthma Onset in Menopausal Women: National Cohort Study

Syed A Shah 1 , Holly Tibble 2 , Rebecca Pillinger 2 , Susannah McLean 2 , Dermot Ryan, Hilary Critchley et al.

**Background:** There is uncertainty about the role of hormonal replacement therapy (HRT) in development of asthma. **Objective:** We investigated whether use of HRT and duration of use was associated with risk of developing asthma in peri- and post-menopausal women. **Methods:** We constructed a 17-year (1/1/2000 - 12/31/2016) open cohort of 353,173 women (46-70 years old) from the Optimum Patient Care Database, a longitudinal primary care database from across UK. HRT use, subtypes, and duration of use; confounding variables; and asthma onset were defined using the Read Clinical Classification System. We fitted multilevel Cox regression models to estimate hazard ratios (HR) with 95% confidence intervals (CIs). **Results:** During 17-year follow-up (1,340,423 person-years), 7,614 new asthma cases occurred, giving an incidence rate of 5.7 (95%CI 5.5-5.8) per 1,000 person-years. Compared to non-use of HRT, previous use of any (HR 0.83; 95%CI 0.76-0.88), estrogen-only (HR 0.89; 95%CI 0.84-0.95), and combined estrogen/progestogen (HR 0.82; 95%CI 0.76-0.88) HRT were associated with a reduced risk of asthma onset. This was also the case with current use of any (HR 0.79; 95%CI 0.74-0.85), estrogen-only (HR 0.80; 95%CI 0.73-0.87), and combined estrogen/progestogen (HR 0.78; 95%CI 0.70-0.87) HRT. Longer duration of HRT use (1-2 years: HR 0.93; 95%CI 0.87-0.99; 3-4 years: HR 0.77; 95%CI 0.70-0.84; 5+ years: HR 0.71; 95%CI 0.64-0.78) was associated with a dose-response reduced risk of asthma onset. **Conclusion:** We found that HRT was associated with a reduced risk of developing late onset asthma in menopausal women. Further cohort studies are needed to confirm these findings.

**Sci Rep. 2020 Dec 4;10(1):21258.doi: 10.1038/s41598-020-77871-9.**

### Longitudinal changes in reproductive hormones through the menopause transition in the Avon Longitudinal Study of Parents and Children (ALSPAC)

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We characterised changes in reproductive hormones-LH, FSH, SHBG and AMH-by chronological age and time around the menopause (reproductive age) in mid-life women and explored their associations with lifestyle and reproductive factors. We used data from 1608 women from a UK cohort who had repeat hormone measures and experienced a natural

menopause. Multilevel models were used to assess: (i) changes in hormones (outcomes) by reproductive age and chronological age (these age variables being the key exposures) and (ii) associations of body mass index (BMI), smoking, alcohol intake, parity and age at menarche with changes in hormones by reproductive age. Both LH and FSH increased until ~ 5 and 7 years postmenopause, respectively, after which they declined, but not to premenopausal levels. SHBG decreased slightly until ~ 4 years postmenopause and increased thereafter. AMH decreased markedly before menopause and remained low subsequently. For all hormones, the best fitting models included both reproductive and chronological age. BMI, smoking and parity were associated with hormone changes; e.g., higher BMI was associated with slower increase in LH and FSH and decrease in AMH. Reproductive and chronological age contribute to changes in LH, FSH, SHBG and AMH across mid-life in women, and BMI, smoking and parity are associated with these hormone changes.

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### **Osteosarcopenia: where osteoporosis and sarcopenia collide**

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The coexistence of osteoporosis and sarcopenia has been recently considered in some groups as a syndrome termed 'osteosarcopenia'. Osteoporosis describes low bone mass and deterioration of the micro-architecture of the bone, whereas sarcopenia is the loss of muscle mass, strength and function. With an ageing population the prevalence of both conditions is likely to increase substantially over the coming decades and is associated with significant personal and societal burden. The sequelae for an individual suffering from both conditions together include a greater risk of falls, fractures, institutionalization and mortality. The aetiology of 'osteosarcopenia' is multifactorial with several factors linking muscle and bone function, including genetics, age, inflammation and obesity. Several biochemical pathways have been identified that are facilitating the development of several promising therapeutic agents, which target both muscle and bone. In the current review we outline the epidemiology, pathogenesis and clinical consequences of 'osteosarcopenia' and explore current and potential future management strategies.

**ArteriosclerThromb Vasc Biol. 2020 Dec 3.doi: 10.1161/ATVBAHA.120.315355. Online ahead of print.**

### **HDL (High-Density Lipoprotein) Subclasses, Lipid Content, and Function Trajectories Across the Menopause Transition: SWAN-HDL Study**

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Objective: The cardioprotective capacity of HDL (high-density lipoprotein) cholesterol postmenopause has been challenged. HDL subclasses, lipid contents, and function might be better predictors of cardiovascular risk than HDL cholesterol. Changes in these measures have not been characterized over the menopause transition (MT) with respect to timing relative to the final menstrual period. Approach and Results: Four hundred seventy-one women with HDL particle (HDL-P) subclasses (nuclear magnetic resonance spectroscopy total, large, medium, and small HDL-P and HDL size), HDL lipid content (HDL phospholipids and triglycerides), and HDL function (cholesterol efflux capacity [HDL-CEC]) measured for a maximum of 5 time points across the MT were included. HDL cholesterol and total HDL-P increased across the MT. Within the 1 to 2 years bracketing the final menstrual period, large HDL-P and HDL size declined while small HDL-P and HDL-triglyceride increased. Although overall HDL-CEC increased across the MT, HDL-CEC per HDL-P declined. Higher concentrations of total, large, and medium HDL-P and greater HDL size were associated with greater HDL-CEC while of small HDL-P were associated with lower HDL-CEC. Associations of large HDL-P and HDL size with HDL-CEC varied significantly across the MT such that higher large HDL-P concentrations and greater HDL size were associated with lower HDL-CEC within the 1 to 2 years around the final menstrual period. Conclusions: Although HDL cholesterol increased over the MT, HDL subclasses and lipid content showed adverse changes. While overall HDL-CEC increased, HDL-CEC per HDL-P declined, consistent with reduced function per particle. Large HDL-P may become less efficient in promoting HDL-CEC during the MT.

**Gynecol Endocrinol. 2020 Dec 2;1-6. doi: 10.1080/09513590.2020.1852544. Online ahead of print.**

### **Management of perimenopause disorders: hormonal treatment**

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Perimenopause represents a transition period of a woman's life during which physiological, affective, psychological, and social changes mark progression from a woman's fertile life to menopause, with wide sexual hormones fluctuations

until the onset of hypergonadotropic hypogonadic amenorrhea. Contraception during menopause should not only avoid unwanted pregnancies, but also improve quality of life and prevent wide range of condition affecting this population. Hormonal contraceptives confer many noncontraceptive benefits for women approaching menopause: treatment of abnormal uterine bleeding, relief from vasomotor symptoms, endometrial protection in women using estrogen therapy, musculoskeletal protection, and mood disorders protection. The main point remains selecting the most adequate contraceptive option for each woman, considering her risk factor, comorbidities, and keeping in mind the possibility of continuing contraception until reaching menopause and even further, creating a bridge between perimenopause and menopause hormonal therapy. Correct perimenopause management should rely on individualized medical therapy and multidisciplinary approach considering lifestyle and food habits as part of general good health of a woman.

**AIMS Neurosci. 2020 Oct 30;7(4):401-417.doi: 10.3934/Neuroscience.2020025. eCollection 2020.**

## **Neuroimmunomodulation by estrogen in health and disease**

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Systemic homeostasis is maintained by the robust bidirectional regulation of the neuroendocrine-immune network by the active involvement of neural, endocrine and immune mediators. Throughout female reproductive life, gonadal hormones undergo cyclic variations and mediate concomitant modulations of the neuroendocrine-immune network. Dysregulation of the neuroendocrine-immune network occurs during aging as a cumulative effect of declining neural, endocrine and immune functions and loss of compensatory mechanisms including antioxidant enzymes, growth factors and co-factors. This leads to disruption of homeostasis and sets the stage for the development of female-specific age-associated diseases such as autoimmunity, osteoporosis, cardiovascular diseases and hormone-dependent cancers. Ovarian hormones especially estrogen, play a key role in the maintenance of health and homeostasis by modulating the nervous, endocrine and immune functions and thereby altering neuroendocrine-immune homeostasis. Immunologically estrogen's role in the modulation of Th1/Th2 immune functions and contributing to pro-inflammatory conditions and autoimmunity has been widely studied. Centrally, hypothalamic and pituitary hormones influence gonadal hormone secretion in murine models during onset of estrous cycles and are implicated in reproductive aging-associated acyclicity. Loss of estrogen affects neuronal plasticity and the ensuing decline in cognitive functions during reproductive aging in females implicates estrogen in the incidence and progression of neurodegenerative diseases. Peripherally, sympathetic noradrenergic (NA) innervations of lymphoid organs and the presence of both adrenergic (AR) and estrogen receptors (ER) on lymphocytes poise estrogen as a potent neuroimmunomodulator during health and disease. Cyclic variations in estrogen levels throughout reproductive life, perimenopausal surge in estrogen levels followed by its precipitous decline, concomitant with decline in central hypothalamic catecholaminergic activity, peripheral sympathetic NA innervation and associated immunosuppression present an interesting study to explore female-specific age-associated diseases in a new light.

**PLoS One. 2020 Dec 1;15(12):e0243037.doi: 10.1371/journal.pone.0243037. eCollection 2020.**

## **Hysterectomies are associated with an increased risk of osteoporosis and bone fracture: A population-based cohort study**

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**Aim:** This study investigated the risk of osteoporosis or bone fractures (vertebrae, hip and others) in hysterectomized women in Taiwan. **Materials and methods:** This is a retrospective population-based cohort study from 2000 to 2013. Women aged  $\geq 30$  years who underwent hysterectomy between 2000 and 2012 were included in this study. The comparison group was randomly selected from the database with a 1:4 matching with age and index year. Incidence rate and hazard ratios of osteoporosis and bone fracture between hysterectomized women and the comparison group were calculated. Cox proportional hazard regressions were used to calculate hazard ratios (HRs) and 95% confidence intervals (CIs). **Results:** We identified 9,189 hysterectomized women and 33,942 age-matched women without a hysterectomy. All women were followed for a median time of about 7 years. The adjusted hazard ratio (aHR) of subsequent osteoporosis or bone fracture was higher in the hysterectomy women (2.26, 95% confidence interval [CI] = 2.09-2.44) than in the comparison group. In the subgroup analysis, oophorectomy and estrogen therapy increase the risk of osteoporosis or fracture in both groups. Regarding the fracture site, the aHR of vertebral fracture (4.92, 95% CI = 3.78-6.40) was higher in the hysterectomized women than in the comparison group. As follow-up time increasing, the aHR of vertebral fracture in hysterectomized women were 4.33 (95% CI = 2.99-6.28), 3.89 (95% CI = 2.60-5.82) and 5.42 (95% CI = 2.66-11.01) for  $< 5$ , 5-9 and  $\geq 9$  years of follow-up, respectively. **Conclusions:** In conclusion, we found that hysterectomized women might be associated with increased risks of developing osteoporosis or bone fracture.

**Climacteric. 2020 Dec;23(6):525-527. doi: 10.1080/13697137.2020.1837547.**

## **The severe acute respiratory syndrome due to coronavirus 2 (SARS-CoV-2) infection and the climacteric woman**

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The severe acute respiratory syndrome due to coronavirus 2 (SARS-CoV-2) infection has affected millions of individuals worldwide, causing high mortality rates and severe physical sequelae, with a negative impact on society, economy, health care, lifestyle and personal relationships. Studies have confirmed this infection has sex and age differences in terms of disease severity and immune response, with a particular relationship with the anti-Müllerian hormone, a marker of aging, and estradiol, a marker of ovarian function. Postmenopausal women seem to present a more severe infection as compared to premenopausal ones. Estradiol protects the vascular system, mediating with the renin-angiotensin-aldosterone system, whereas testosterone enhances the levels of angiotensin-converting enzyme and the transmembrane protease serine-type 2, thus delaying viral clearance in men as compared to women. This new infection will stay among us, transforming our social, economic and daily lifestyle, and hence medical and health care as well as the use of menopause hormone therapy will need redefining, considering both preventive and curative perspectives.

**Circulation. 2020 Nov 30;CIR000000000000912.doi: 10.1161/CIR.000000000000912. Online ahead of print.**

## **Menopause Transition and Cardiovascular Disease Risk: Implications for Timing of Early Prevention: A Scientific Statement From the American Heart Association**

Samar R El Khoudary, Brooke Aggarwal, Theresa M Beckie, Howard N Hodis, Amber E Johnson, Robert D Langer, Marian C Limacher, JoAnn E Manson, Marcia L Stefanick, Matthew A Allison, American Heart Association Prevention Science Committee of the Council on Epidemiology and Prevention; and Council on Cardiovascular and Stroke Nursing

Cardiovascular disease (CVD) is the leading cause of death in women, who have a notable increase in the risk for this disease after menopause and typically develop coronary heart disease several years later than men. This observation led to the hypothesis that the menopause transition (MT) contributes to the increase in coronary heart disease risk. Over the past 20 years, longitudinal studies of women traversing menopause have contributed significantly to our understanding of the relationship between the MT and CVD risk. By following women over this period, researchers have been able to disentangle chronological and ovarian aging with respect to CVD risk. These studies have documented distinct patterns of sex hormone changes, as well as adverse alterations in body composition, lipids and lipoproteins, and measures of vascular health over the MT, which can increase a woman's risk of developing CVD postmenopausally. The reported findings underline the significance of the MT as a time of accelerating CVD risk, thereby emphasizing the importance of monitoring women's health during midlife, a critical window for implementing early intervention strategies to reduce CVD risk. Notably, the 2011 American Heart Association guidelines for CVD prevention in women (the latest sex-specific guidelines to date) did not include information now available about the contribution of the MT to increased CVD in women. Therefore, there is a crucial need to discuss the contemporary literature on menopause and CVD risk with the intent of increasing awareness of the significant adverse cardiometabolic health-related changes accompanying midlife and the MT. This scientific statement provides an up-to-date synthesis of the existing data on the MT and how it relates to CVD.