

## Selección de Resúmenes de Menopausia

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María Soledad Vallejo. Clínica Quilín. Universidad de Chile

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### **Menstrual cycle characteristics and incident cancer: a prospective cohort study**

Siwen Wang 1 2, Yi-Xin Wang 1, Helena Sandoval-Insausti 1, Leslie V Farland 3, Jan L Shifren 4, et al.

**Study question:** Are menstrual cycle characteristics throughout the reproductive lifespan associated with cancer risk?  
**Summary answer:** Irregular and long menstrual cycles throughout the reproductive lifespan were associated with increased risk of total invasive cancer, especially obesity-related cancers. What is known already: Long and irregular menstrual cycles have been associated with lower risk of pre-menopausal breast cancer and higher risk of endometrial cancer, but associations with other malignancies are less clear. **Study design, size, duration:** Prospective cohort study. **Prospective follow-up of** 78 943 women participating in the Nurses' Health Study II between 1989 and 2015. **Participants/materials, setting, methods:** We followed 78 943 pre-menopausal women without cancer history who reported the usual length and regularity of their menstrual cycles at different ages (14-17, 18-22 and 29-46 years). Cancer diagnosis was confirmed through medical record review and classified as obesity-related (colorectal, gallbladder, kidney, multiple myeloma, thyroid, pancreatic, esophageal, gastric, liver, endometrial, ovarian and post-menopausal breast) or non-obesity-related. We fitted Cox proportional hazards models to estimate hazard ratios (HRs) and 95% CIs of the association between menstrual cycle characteristics and cancer incidence. **Main results and the role of chance:** We documented 5794 incident cancer cases during 1 646 789 person-years of follow-up. After adjusting for BMI and other potential confounders, women reporting irregular cycles at age 29-46 years had an 11% (95% CI: 2-21%) higher risk of total invasive cancer than women reporting very regular cycles at the same age. This association was limited to obesity-related cancers, with a 23% (95% CI: 9-39%) higher risk and was strongest for endometrial cancer (HR = 1.39; 95% CI: 1.09-1.77). Findings were comparable for cycle characteristics earlier in life and for menstrual cycle length. Very irregular cycles at age 14-17 years were associated with significant increase in risk of colorectal cancer (HR = 1.36; 95% CI: 1.02-1.81). **Limitations, reasons for caution:** Our study might be subject to recall bias for findings pertaining to cycle characteristics in adolescence and early adulthood, as these were retrospectively reported. Generalizability to non-White women may be limited, as 96% of participants were White. **Wider implications of the findings:** Women with irregular or long menstrual cycles in mid-adulthood had a statistically significantly higher risk of developing cancer, especially obesity-related cancers. This association was not limited to gynecological cancers. Obesity-related cancers may need to be added to the spectrum of long-term health consequences of long or irregular cycles, possibly warranting targeted screening among women who experience long or irregular cycles in mid-adulthood.

**Post Reprod Health. 2021 Dec 10;20533691211063342. doi: 10.1177/20533691211063342. Online ahead of print.**

### **Arterial hypertension in women: Menopause as a risk window**

Basil N Okeahialam 1, Hadiza Agbo 2, Evelyn Chuhwak 1, Ikechukwu Isiguzoro 3

**Objectives:** Cardiovascular diseases (CVD) exert a heavy toll on health of women, mainly due to hypertension said to cluster around the period of transition to menopause. This makes this period a good window to target for prevention and control. We therefore sought to determine if this period really heralds arterial hypertension and CVD in women in our environment. **Study design:** We secondarily analysed our population data on CVD risk factors in free living rural residents. **Main outcome variables:** The data considered were blood pressure, anthropometric and biochemical variables in women stratified based on menstruation status. **Results:** There were 488 females, with 218 still menstruating. They were younger ( $p = .000$ ), had lower systolic and diastolic blood pressures ( $p = .000$ ), lower anthropometric indices attaining significance only with waist circumference ( $p = .001$ ) and lower total cholesterol ( $p = .001$ ). Controlling for age, statistically significant differences remained for systolic and diastolic blood pressures, body mass index, waist and hip circumferences, and total cholesterol. **Conclusion:** The menopause transition comes with a worse CVD profile. Blood pressure rises and so are the anthropometric variables and some biochemical parameters that fuel CVD. This could be ascribed to age which is higher with those post-menopausal. Controlling for age in this cohort still showed that transiting from pre- to post-menopause still came with CVD burden. Clinicians should take the opportunity presented by menopause transition to screen for CVD risk factors and initiate either preventive or control measures to mitigate morbi-mortality consequences.

**Arch Environ Occup Health. 2021 Dec 9;1-11. doi: 10.1080/19338244.2021.2007834. Online ahead of print.**

## **Comparison of metabolic syndrome and related factors in married pre-menopausal white- and blue-collar woman**

Seungmi Park 1, Chul-Gyu Kim 1, Youngji Kim 2

This study aimed to identify the prevalence and associated factors of metabolic syndrome in pre-menopausal married women with white-collar and blue-collar jobs. This study analyzed 4,447 women with jobs in the Korean National Health and Nutrition Examination Survey (2010-2018). The prevalence of metabolic syndrome was higher among blue-collar women (15.3%) than among white-collar women (10.5%). Age, family type, alcohol consumption, frequency of high-risk drinking, perceived health status, and body mass index (BMI) were significantly associated with metabolic syndrome in the white-collar (p < .05). Age, family type, frequency of eating out, and BMI were associated in the blue-collar (p < .05). Blue-collar women were more vulnerable to metabolic syndrome than white-collar ones. To prevent metabolic syndrome in pre-menopausal married women with jobs, lifestyle modifications such as mitigating obesity and reducing alcohol consumption with aging are necessary.

**Neuropsychiatr Dis Treat. 2021 Dec 2;17:3483-3488. doi: 10.2147/NDT.S333154. eCollection 2021.**

## **Reduced Plasma Estradiol Levels are Associated with Sleep Apnea in Depressed Peri- and Post-Menopausal Women**

Li-Qiang Cai 1 2, Lei Huang 1 2, Li-Li Wei 1 2, Jia-Shu Yao 1 2, Luo-Yi Xu 1 2, Wei Chen 1 2

**Objective:** This study aimed at investigating the correlation between estradiol and sleep apnea among women with major depressive disorders during the perimenopausal and postmenopausal periods. **Methods:** A total of 84 perimenopausal and postmenopausal women diagnosed with depression, and who had been subjected to whole-night polysomnography (PSG) were retrospectively studied. They were assigned into two groups based on the presence of OSA (apnea-hypopnea index (AHI)  $\geq 5$ ) (OSA vs non-OSA). The correlation between estradiol levels and apnea-hypopnea index were assessed by logistic regression models after adjusting for age, body mass index (BMI), Hamilton Depression Rating Scale (HAMD), Pittsburgh Sleep Quality Index (PSQI), apnea frequency and progesterone. **Results:** Among the 84 patients, 45.23% had OSA. Estradiol levels were significantly elevated in non-OSA than in OSA patients (p < 0.05). Univariate analysis revealed that elevated estradiol levels are associated with reduced odds of OSA (odds ratio [OR] 0.92, 95% confidence interval [CI] 0.875-0.966, p = 0.001). Multivariate analyses showed that low estradiol levels (OR = 0.859, 95% CI 0.826-0.991, p = 0.031), higher HAMD scores (OR = 1.212, 95% CI 1.012-1.453, p = 0.037), higher apnea frequency (OR = 2.493, 95% CI 1.389-4.473, p = 0.002) and higher BMI (OR = 1.635, 95% CI 1.136-2.353, p = 0.008) are correlated with OSA. **Conclusion:** The ratio of depressed perimenopausal to postmenopausal women comorbid OSA was high. Higher BMI, low estradiol levels, high apnea frequency and high HAMD scores were correlated with OSA diagnosis and could be potential diagnostic markers for OSA in depressed perimenopausal and postmenopausal women. Reduced estradiol levels were correlated with an increased risk of OSA among depressed perimenopausal and postmenopausal women.

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## **Association of bilateral salpingo-oophorectomy with all cause and cause specific mortality: population based cohort study**

Maria C Cusimano 1 2, Maria Chiu 2 3, Sarah E Ferguson 1 4, Rahim Moineddin 3 5 6, Suriya Aktar 3, et al.

**Objectives:** To determine if bilateral salpingo-oophorectomy, compared with ovarian conservation, is associated with all cause or cause specific death in women undergoing hysterectomy for non-malignant disease, and to determine how this association varies with age at surgery. **Design:** Population based cohort study. **Setting:** Ontario, Canada from 1 January 1996 to 31 December 2015, and follow-up to 31 December 2017. **Participants:** 200 549 women (aged 30-70 years) undergoing non-malignant hysterectomy, stratified into premenopausal (<45 years), menopausal transition (45-49 years), early menopausal (50-54 years), and late menopausal ( $\geq 55$  years) groups according to age at surgery; median follow-up was 12 years (interquartile range 7-17). **Exposures:** Bilateral salpingo-oophorectomy versus ovarian conservation. **Main outcomes measures:** The primary outcome was all cause death. Secondary outcomes were non-cancer and cancer death. Within each age group, overlap propensity score weighted survival models were used to examine the association between bilateral salpingo-oophorectomy and mortality outcomes, while adjusting for demographic characteristics, gynaecological conditions, and comorbidities. To account for comparisons in four age groups, P < 0.0125 was considered statistically significant. **Results:** Bilateral salpingo-oophorectomy was performed in

19%, 41%, 69%, and 81% of women aged <45, 45-49, 50-54, and  $\geq 55$  years, respectively. The procedure was associated with increased rates of all cause death in women aged <45 years (hazard ratio 1.31, 95% confidence interval 1.18 to 1.45,  $P < 0.001$ ; number needed to harm 71 at 20 years) and 45-49 years (1.16, 1.04 to 1.30,  $P = 0.007$ ; 152 at 20 years), but not in women aged 50-54 years (0.83, 0.72 to 0.97,  $P = 0.018$ ) or  $\geq 55$  years (0.92, 0.82 to 1.03,  $P = 0.16$ ). Findings in women aged <50 years were driven largely by increased non-cancer death. In secondary analyses identifying a possible change in the association between bilateral salpingo-oophorectomy and all cause death with advancing age at surgery, the hazard ratio gradually decreased during the menopausal transition and remained around 1 at all ages thereafter. Conclusion: In this observational study, bilateral salpingo-oophorectomy at non-malignant hysterectomy appeared to be associated with increased all cause mortality in women aged <50 years, but not in those aged  $\geq 50$  years. While caution is warranted when considering bilateral salpingo-oophorectomy in premenopausal women without indication, this strategy for ovarian cancer risk reduction does not appear to be detrimental to survival in postmenopausal women.

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## **The Effect of Exogenous Sex Steroids on the Vaginal Microbiota: A Systematic Review**

Larissa K Ratten<sup>1 2</sup>, Erica L Plummer<sup>1 2</sup>, Catriona S Bradshaw<sup>1 2 3</sup>, Christopher K Fairley<sup>1 2</sup>, et al.

**Background:** Exogenous sex steroids within hormonal contraception and menopausal hormone therapy (MHT) have been used for family planning and management of menopausal symptoms, without consideration of their effects on the vaginal microbiota. This is largely because their use predates our understanding of the importance of the vaginal microbiome on human health. We conducted a systematic review (PROSPERO: CRD42018107730) to determine the influence of exogenous sex steroids, stratified by oestrogen-containing or progestin-only types of contraception, and MHT on the vaginal microbiome, as measured by molecular methods. **Methods:** Embase, PubMed and Medline were searched for relevant literature published through to December 1st 2020. Eligible studies reported on the effect of specific exogenous sex steroids on the vaginal microbiome using a molecular method. Data regarding the 'positive', 'negative' or 'neutral' effect of each type of contraceptive or MHT on the vaginal microbiome was extracted and summarised. A positive effect reflected sex steroid exposure that was associated with increased abundance of lactobacilli, a change to, or maintenance of, an optimal vaginal microbiota composition, or a decrease in bacterial diversity (specifically reflecting a low-diversity optimal microbiota state), relative to the control group. An exogenous sex steroid was designated as having a negative effect on the vaginal microbiome if it resulted in opposing effects (i.e. loss of lactobacilli, a non-optimal microbiota state). When no significant change was found, this was considered neutral/inconclusive. **Results:** We identified 29 manuscripts reporting on the effect of exogenous sex steroids on the vaginal microbiome; 25 investigating hormonal contraceptives, and 4 investigating MHT. Oestrogen-containing contraception, particularly reflecting the combined oestrogen and progestin-containing contraceptive pill, had a positive effect on the composition of the vaginal microbiota. Progestin-only contraception, particularly reflecting depot-medroxyprogesterone acetate, had mixed effects on the microbiota. Among post-menopausal women using MHT, exogenous oestrogen applied topically was associated with increased prevalence of lactobacilli. **Conclusion:** Our findings suggest that oestrogen-containing compounds may promote an optimal vaginal microbiota, which could have clinical applications. The impact of progestin-only contraceptives on the vaginal microbiota is less clear; more data is needed to determine how progestin-only contraceptives contribute to adverse reproductive and sexual health outcomes.