

Selección de Resúmenes de Menopausia

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María Soledad Vallejo. Obstetricia Ginecología. Hospital Clínico. Universidad de Chile

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Body mass index and breast cancer risk among postmenopausal women with and without cardiometabolic diseases: Findings from two prospective cohort studies in Europe

Emma Fontvieille 1, Anna Jansana 1, Laia Peruchet-Noray, Reynalda Córdova, Quan Gan, Sabina Rinaldi, et al. Background: Adiposity, measured by body mass index (BMI), is a known risk factor for postmenopausal breast cancer. However, whether the association of BMI with breast cancer risk differs among women with and without cardiovascular diseases (CVDs) or type 2 diabetes (T2D) is uncertain. Methods: This study used individual participant data from the European Prospective Investigation into Cancer and Nutrition (EPIC) and UK Biobank (UKB) that included 168,547 postmenopausal women who were free of cancer, T2D, and CVD at recruitment. Hazard ratios (HRs) and 95% confidence intervals (CIs) were estimated with multivariable-adjusted Cox regression for associations between BMI and incident breast cancer by T2D and CVD status. Incidence rates per 1000 person-years and rate differences between observed and expected joint associations of adiposity and CVD or T2D for breast cancer were estimated. Study-specific estimates were meta-analyzed. Results: After a median follow-up of 10.7 years in EPIC and 10.9 years in UKB, 6793 postmenopausal women developed breast cancer. In the meta-analysis of both cohorts, BMI (per 1-SD increment, 5 kg/m²) was more strongly associated with breast cancer risk in women with CVD (HR, 1.31; 95% CI, 1.16 to 1.47) than in women without CVD (HR, 1.13; 95% CI, 1.11 to 1.16) (pinteraction = .02). T2D did not modify breast cancer risk (pinteraction = .33). The meta-analyzed joint association of overweight or obesity (BMI, ≥25 kg/m²) and CVD led to 1.53 (95% CI, 0.35 to 2.71) more cases of breast cancer per 1000 person-years than expected but no such joint association was observed with T2D. Conclusions: Adiposity-associated risk of breast cancer was substantially higher among women with CVD as compared to those without CVD.

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Vaginal CO2 laser treatment for urinary stress incontinence: A randomized controlled trial

Hrefna Bóel Sigurdardóttir 1, Benny Kirschner 2, Josephine Obel 3, Mubeena Aziz 4, Cathrine Blegvad Stenz 5, et al. Objectives: The effect of laser treatment for stress urinary incontinence is inconclusive. The aim of this study was to determine the efficacy and safety of vaginal CO2 laser in women with stress urinary incontinence. Study design: Single-site, patient-blinded, placebo-controlled randomized trial at Hvidovre University Hospital, Denmark. Thirty-seven women with mild to severe symptoms of stress urinary incontinence were included. They were randomized to either laser or sham treatment and received three treatments, four weeks apart. At first and last visit, the women completed the ICIQ-UI SF questionnaire and had a standardized urinary stress test. Both groups received supervised pelvic floor muscle training, and postmenopausal women were recommended vaginal estrogen treatment. Main outcome measures: The primary outcome was post-treatment score on the International Consultation on Incontinence Questionnaire-Urinary Incontinence Short Form (ICIQ-UI SF). Scores were compared using Student's t-test and 95 % confidence intervals (CI). The secondary outcome was performance on the post-treatment standardized stress test. Results: Baseline characteristics did not differ between the groups. There was no difference in ICIQ-IU SF scores post-treatment between the two groups: mean score for the laser group 12.2 vs. 12.7 for sham (mean difference 95 % CI: -2.15 to 3.15; p-value 0.70). Likewise, we found no difference between the groups in performance on the post-treatment standardized stress test (95 % CI: -4.33 g to 40.73 g; p-value 0.11). One adverse event occurred, a bladder infection that required hospital admission. Conclusions: In this study, CO2 vaginal laser did not improve the symptoms of stress urinary incontinence. It is acknowledged that the study population was small.

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Hormone therapy use and young-onset breast cancer: a pooled analysis of prospective cohorts included in the Premenopausal Breast Cancer Collaborative Group

Katie M O'Brien 1, Melissa G House 2, Mandy Goldberg 3, Michael E Jones 4, Clarice R Weinberg 5, et al.

Background: Oestrogen plus progestin hormone therapy is an established risk factor for breast cancer in postmenopausal women. We examined the less well-studied association between exogenous hormones and breast cancer in young women, who might use hormone therapy after gynaecological surgery or to relieve perimenopausal symptoms. **Methods:** In this pooled cohort analysis, we investigated the relationship between exogenous hormones and breast cancer in young women using data from 10-13 prospective cohorts from North America, Europe, Asia, and Australia. The participating cohorts followed up women for incident breast cancer until age 55 years. We used cohort-stratified, multivariable-adjusted Cox proportional hazards regression to estimate hazard ratios (HRs) and 95% CI for associations of hormone therapy with incident young-onset breast cancer. We also estimated risk differences based on cumulative risk until age 55 years. **Findings:** We included 459 476 women aged 16-54 years (mean 42.0 years [IQR 35.5-49.2]), of whom 8455 (2%) developed young-onset breast cancer (diagnosed before age 55 years; median follow-up 7.8 years [5.2-11.2]). Overall, 15% of participants reported using hormone therapy, with oestrogen plus progestin hormone therapy (6%) and unopposed oestrogen (5%) being the most common types. Cumulative risk of young-onset breast cancer was 4.1% in non-users. Hormone therapy of any type was not associated with incident young-onset breast cancer (HR 0.96 [95% CI 0.88 to 1.04]), but ever oestrogen hormone therapy use was inversely associated (0.86 [0.75 to 0.98]; risk difference -0.5% [-1.0 to -0.0]). The HR for ever oestrogen plus progestin hormone therapy and young-onset breast cancer was 1.10 (0.98 to 1.24), with positive associations observed for long-term use (1.18 [1.01 to 1.38] for >2 years) and use among women without hysterectomy or bilateral oophorectomy (1.15 [1.02 to 1.31]). Oestrogen hormone therapy and young-onset breast cancer association was similar for all breast cancer subtypes, but oestrogen plus progestin hormone therapy was more strongly associated with oestrogen receptor negative (1.44 [1.11 to 1.88]) and triple-negative disease (1.50 [1.02 to 2.20]) than with other subtypes. **Interpretation:** Oestrogen hormone therapy use was inversely associated with young-onset breast cancer, and oestrogen plus progestin hormone therapy was associated with higher young-onset breast cancer incidence among women with intact uterus and ovaries. These findings largely parallel results from studies of hormone use and later-onset breast cancer and provide novel evidence for establishing clinical recommendations among younger women.

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Sitting time and risk of cancer incidence and cancer mortality in postmenopausal women: the Women's Health Accelerometry Collaboration

Eric T Hyde 1 2, Kelly R Evenson 3, Annie Green Howard 4 5, Humberto Parada Jr 6, Chongzhi Di 7, et al.

Purpose: Few studies have explored whether accelerometer-measured sedentary behavior increases cancer risk. We examined the associations of accelerometer-measured daily sitting time and mean sitting bout duration classified by the Convolutional Neural Network Hip Accelerometer Posture (CHAP) machine-learned algorithm with incidence of any cancer, incidence of 13 physical activity-related cancers, and cancer mortality among postmenopausal women. **Methods:** We used data from 22,097 women (mean age = 73.3 years, standard deviation [SD] = 6.7) in the Women's Health Accelerometry Collaboration, a consortium of two US-based cohort studies of postmenopausal women: the Women's Health Study and the Women's Health Initiative Objective Physical Activity and Cardiovascular Health Study. Women who completed hip-worn triaxial accelerometry for ≥ 4 of 7 consecutive days were included. Associations between sedentary behaviors and physician-adjudicated invasive cancer incidence and mortality were tested using Cox regression. **Results:** Women were followed on average 8.0 years to identify cancer cases ($n = 1,861$) and deaths ($n = 601$). Overall, mean sitting time was 567 (SD = 113) min/day and mean sitting bout duration was 12.8 (SD = 4) min/bout. In covariate-adjusted models, one-SD increment higher in sitting time was associated with a 6% increased risk of incident cancer (hazard ratio [HR] = 1.06, 95% CI: 1.01-1.11); associations were similar for bout duration (HR = 1.05, 95% CI: 1.00-1.10). Estimates were similar for the 13 physical activity-related cancers (sitting time: HR = 1.10, 95% CI: 1.04-1.17; bout duration: HR = 1.08, 95% CI: 1.02-1.14) and for cancer mortality (sitting time: HR = 1.06, 95% CI: 0.98-1.16; bout duration: HR = 1.05, 95% CI: 0.97-1.13). **Conclusion:** Among postmenopausal women, sedentary behavior was associated with increased cancer risk, particularly for physical activity-related cancers and cancer mortality.

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Pharmacological Treatments for Menopausal Vasomotor Symptoms: A Systematic Review and Bayesian Network Meta-Analysis of Efficacy and Safety

Wellgner Fernandes Oliveira Amador 1, Cainã Araújo Saraiva 2, Mariano Gallo Ruelas 3, Ivo Queiroz 4, et al.

Objectives: To evaluate the efficacy and safety of pharmacological treatments for vasomotor symptoms (VMS) in postmenopausal women. **Methods:** A systematic search was conducted in PubMed, Embase, and the Cochrane Library through January 2025. Eligible studies were Phase 3 or 4 randomized controlled trials (RCTs) assessing pharmacological treatments for moderate to severe VMS with ≥ 12 weeks of follow-up. A Bayesian random-effects network meta-analysis estimated mean differences (MDs) and risk ratios (RRs) with 95 % credible intervals (CrI). Treatments were ranked using surface under the cumulative ranking (SUCRA). Risk of bias was assessed using Cochrane's tool. **Results:** Forty-one RCTs ($n = 14,743$; mean age 53.4 years) were included. Synthetic conjugated estrogens (SCE) 1.25 mg showed the greatest reduction in VMS frequency (MD -5.69; 95 % CrI -7.93 to -3.38), while drospirenone 0.5 mg + estradiol 0.5 mg was most effective for severity (MD -1.06; 95 % CrI -1.39 to -0.72). Most treatments had safety profiles similar to placebo, though estradiol 0.5 mg + dydrogesterone 2.5 mg was linked to more adverse events (RR 1.56; 95 % CrI 1.16 to 2.24). No significant differences in serious adverse events were found. SUCRA rankings highlighted SCE and transdermal estradiol gel as most effective for frequency, while drospirenone + estradiol led for severity. Fezolinetant and elinzanetant showed moderate efficacy. Of the studies, 22 had low risk of bias, and 19 had some concerns. **Conclusions:** Conjugated estrogens and drospirenone with estradiol are the most effective options for reducing VMS frequency and severity, and Fezolinetant and Elinzanetant showed moderate efficacy, with overall similar safety across treatments.

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"I did not recognize myself": a mixed methods study to better understand the experiences of menopause in a US workplace

Sharon Mallen 1, Jennifer Coppola 1, Nicole Shaffer 1, Mary Jane Minkin 2, Alexis Ward 3, Sally Snow 3

Objective: This mixed-methods study aimed to describe the prevalence and impact of menopausal symptoms on midlife women in a US workplace. **Methods:** An online survey was disseminated to all US-based employees of a US-headquartered pharmaceutical company. Eligible respondents were aged 40-65 years and self-identified as having (or expecting to have) personal experience of menopause. Descriptive statistics were generated. Survey respondents were sampled for in-depth interviews, on which thematic analysis was performed. **Results:** Eligible survey responses were received from 1,642 employees, of which 18 participated in in-depth interviews. The mean respondent age was 51 years, and a range of job roles were represented. The majority of respondents (83%) reported that they had current or prior experience of menopause. Menopause symptoms most commonly impacting workplace performance included changes to sleep patterns, changes to memory, hot flashes and anxiety, although interviews highlighted a diversity of symptom presentations. Menopause symptoms were reported to affect stress levels, confidence in abilities, patience with others, and ability to concentrate at work; 7% of menopausal respondents took time off work due to menopause symptoms. Although half of the respondents disclosed that they would feel extremely or somewhat comfortable discussing menopause with colleagues, only 9% of those with current symptoms reported that they had received support with their menopause symptoms at work. **Conclusions:** This study found that menopause impacts women's perceptions of their own performance at work, and that many are unsure how to approach conversations about menopause in the workplace. A substantial gap in knowledge about menopause was identified, highlighting the need for further education and support.

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The rediscovery of estetrol and its implications for estrogen treatment

Herjan J T Coelingh Bennink 1, Roger Gosden 2, Frank Z Stanczyk 3, Eli Y Adashi 4

Objectives: To summarize the literature on the rediscovery and clinical exploration of the fourth natural estrogen estetrol (E4), more than 100 years after the discovery of estrone (E1), estradiol (E2), and estriol (E3). **Methods:** Literature review of E4 publications. **Results:** Preclinical and clinical research and development of E4 revealed that: (1) contrary to the other 3 natural estrogens, E4 has a high oral bioavailability, and (2) oral E4 has limited effect on hemostasis and other liver functions, and is, therefore, expected to be a safer estrogen. Since 2022, E4 combined with drospirenone has been registered worldwide as an oral contraceptive. E4 for menopausal hormone therapy is expected

to become available in 2026. Clinical development of the use of E4 for the treatment of advanced breast cancer and advanced prostate cancer is ongoing, and E4 has been proposed as a component of an oral male contraceptive. Conclusion: The recognition of E4 as a useful and safe natural estrogen for human use is expected to change the scene of estrogen treatment in women and men significantly.

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"Forever fertile": ovarian tissue cryopreservation for an extended reproductive lifespan

Claudia Massarotti 1 2, Chiara Selmi 3, Antonio La Marca 4

The global decline in birth rates highlights the need for effective fertility preservation strategies. Even though oocyte cryopreservation is a well-established technique in cancer patients and is increasingly requested for elective fertility preservation, its success is limited by age at freezing and restoration of ovarian activity is not provided. Ovarian tissue cryopreservation is emerging as a promising alternative for both fertility preservation and reproductive lifespan extension. Unlike oocyte cryopreservation, ovarian tissue cryopreservation restores endocrine function, potentially delaying menopause and reducing associated health risks. Although concerns exist regarding graft longevity and surgical invasiveness, recent advancements-such as improved cryopreservation techniques, neovascularization strategies, and minimally invasive approaches-enhance its feasibility. Additionally, ovarian tissue cryopreservation allows for spontaneous conception, reducing the need for assisted reproductive technologies. As demand for reproductive longevity increases, the medical community must address ethical and regulatory implications while refining clinical applications. Integrating ovarian tissue cryopreservation into elective fertility preservation can provide women with more reproductive choices, aligning with advances in longevity medicine. Future research should focus on optimizing graft survival and assessing long-term health outcomes of delayed menopause to fully unlock the potential of ovarian tissue cryopreservation.