



## Selección de Resúmenes de Menopausia

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### **Influence of the levonorgestrel-releasing intrauterine system on the risk of breast cancer: a systematic review**

Aline Zürcher 1, Laura Knabben 2, Heidrun Janka 3, Petra Stute 4

**Purpose:** The intention of this systematic review was to analyze the literature on breast cancer (BC) and the use of the levonorgestrel-releasing intrauterine system (LNG-IUS). **Methods:** The literature was searched in Medline, Embase, Cochrane Library, CINAHL, Web of Science and ClinicalTrials.com and included search terms related to breast cancer and LNG-IUS. After elimination of duplicates, 326 studies could be identified and were assessed according to inclusion and exclusion criteria. In the end, 10 studies met the defined criteria and were included in the systematic review. **Results:** 6 out of the 10 selected studies were cohort studies, three were case-control studies and one a systematic review/meta-analysis. 6 found a positive association between BC and the use of LNG-IUS. One study only found an increased risk for invasive BC in the subgroup of women aged 40-45 years. In contrast, three studies showed no indication of a higher BC risk. **Conclusion:** The results imply an increased BC risk in LNG-IUS users, especially in postmenopausal women and with longer duration of use. Positive effects of the LNG-IUS such as reduced risks for other hormonal cancers have been observed, were, however, not focus of this systematic review. The heterogeneity of the analyzed studies and vast number of confounding factors call for further investigations in this issue. Patients should be advised according to their individual risk profile and hormone-free alternatives may be considered for women with a history of BC.

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### **Effects of transdermal versus oral hormone replacement therapy in postmenopause: a systematic review**

Marina Šprem Goldštajn 1 2, Mislav Mikuš 1 2, Filippo Alberto Ferrari 3, Mariachiara Bosco 4, et al

**Purpose:** To summarize available evidence comparing the transdermal and the oral administration routes of hormone replacement therapy (HRT) in postmenopausal women. **Methods:** We performed a systematic review of the literature on multiple databases between January 1990 and December 2021. We included randomized controlled trials and observational studies comparing the transdermal and oral administration routes of estrogens for HRT in postmenopausal women regarding at least one of the outcomes of interest: cardiovascular risk, venous thromboembolism (VTE), lipid metabolism, carbohydrate metabolism, bone mineral density (BMD), and risk of pre-malignant and malignant endometrial lesions, or breast cancer. **Results:** The systematic literature search identified a total of 1369 manuscripts, of which 51 were included. Most studies were observational and of good quality, whereas the majority of randomized controlled trials presented a high or medium risk of bias. Oral and transdermal administration routes are similar regarding BMD, glucose metabolism, and lipid profile improvements, as well as do not appear different regarding breast cancer, endometrial disease, and cardiovascular risk. Identified literature provides clear evidence only for the VTE risk, which is higher with the oral administration route. **Conclusions:** Available evidence comparing the transdermal and oral administration routes for HRT is limited and of low quality, recommending further investigations. VTE risk can be considered the clearest and strongest clinical difference between the two administration routes, supporting the transdermal HRT as safer than the oral administration route.

**Diabetes Care. 2022 Jun 17;dc220368. doi: 10.2337/dc22-0368. Online ahead of print.**

### **Dietary Protein Sources, Mediating Biomarkers, and Incidence of Type 2 Diabetes: Findings From the Women's Health Initiative and the U.K. Biobank**

Jie Li 1 2, Andrea J Glenn 3 4 5, Qingling Yang 1, Ding Ding 1, Lingling Zheng 1, Wei Bao, Jeannette Beasley, et al.

**Objective:** Whether and how dietary protein intake is linked to type 2 diabetes (T2D) remains unclear. The aim of this study was to investigate the associations of protein intake with development of T2D and the potential mediating roles of T2D biomarkers. **Research design and methods:** We included 108,681 postmenopausal women without T2D at baseline from the Women's Health Initiative (WHI) (primary cohort) and 34,616 adults without T2D from the U.K.

Biobank (UKB) (replication cohort). Cox proportional hazard models were used for estimation of protein-T2D associations. Mediation analysis was performed to assess the mediating roles of biomarkers in case-control studies nested in the WHI. Results: In the WHI, 15,842 incident T2D cases were identified during a median follow-up of 15.8 years. Intake of animal protein was associated with increased T2D risk (hazard ratio in comparing the highest to the lowest quintile = 1.31 [95% CI 1.24-1.37]) and plant protein with decreased risk (0.82 [0.78-0.86]). Intakes of red meat, processed meat, poultry, and eggs were associated with increased T2D risk and whole grains with decreased risk. Findings from the UKB were similar. These findings were materially attenuated after additional adjustment for BMI. Substituting 5% energy from plant protein for animal protein was associated with 21% decreased T2D risk (0.79 [0.74-0.84]), which was mediated by levels of hs-CRP, interleukin-6, leptin, and SHBG. Conclusions: Findings from these two large prospective cohorts support the notion that substituting plant protein for animal protein may decrease T2D risk mainly by reducing obesity-related inflammation.

**Alzheimers Res Ther. 2022 Jun 16;14(1):83. doi: 10.1186/s13195-022-01026-3.**

### **Hormone therapy and the decreased risk of dementia in women with depression: a population-based cohort study**

Hyewon Kim 1, Juhwan Yoo 2, Kyungdo Han 3, Dong-Yun Lee, Maurizio Fava, David Mischoulon, Hong Jin Jeon. Background: The literature has shown depression to be associated with an increased risk of dementia. In addition, hormone therapy can be a responsive treatment option for a certain type of depression. In this study, we examined the association between hormone therapy, including lifetime oral contraceptive (OC) use, and hormone replacement therapy (HRT) after menopause with the occurrence of dementia among female patients with depression. Methods: The South Korean national claims data from January 1, 2005, to December 31, 2018, was used. Female subjects aged 40 years or older with depression were included in the analyses. Information on hormone therapy was identified from health examination data and followed up for the occurrence of dementia during the average follow-up period of 7.72 years. Results: Among 209,588 subjects, 23,555 were diagnosed with Alzheimer's disease (AD) and 3023 with vascular dementia (VD). Lifetime OC usage was associated with a decreased risk of AD (OC use for < 1 year: HR, 0.92 [95% CI, 0.88-0.97]; OC use for ≥ 1 year: HR, 0.89 [95% CI, 0.84-0.94]), and HRT after menopause was associated with a decreased risk of AD (HRT for < 2 years: HR, 0.84 [95% CI, 0.79-0.89]; HRT for 2-5 years: HR, 0.80 [95% CI, 0.74-0.88]; and HRT for ≥ 5 years : HR, 0.78 [95% CI, 0.71-0.85]) and VD (HRT < 2 years: HR, 0.82 [95% CI, 0.71-0.96]; HRT for 2-5 years: HR, 0.81 [95% CI, 0.64-1.02]; and HRT for ≥ 5 years: HR, 0.61 [95% CI, 0.47-0.79]). Conclusions: In this nationwide cohort study, lifetime OC use was associated with a decreased risk of AD, and HRT after menopause was associated with a decreased risk of AD and VD among female patients with depression. However, further studies are needed to establish causality.

**Womens Health (Larchmt). 2022 Jun;31(6):758-761. doi: 10.1089/jwh.2022.0139.**

### **Clinical Update in Women's Heart Disease**

Melissa A McNeil 1 2

The goal in selecting these recent articles was to help identify literature that may change the clinical practice of women's health for practitioners in the primary care setting. Articles were identified by reviewing high-impact medical and women's health journals, national guidelines, ACP JournalWise, and NEJM Journal Watch. In this clinical update, we selected recent publications relevant to the prevention, risk assessment, and diagnosis of cardiovascular disease (CVD) in women. Breastfeeding now has data suggesting a robust reduction in subsequent CVD, and migraine with aura and severe and early- and late-onset hot flashes can now be considered risk factors for CVD. The decision to initiate menopausal hormone therapy is influenced by estimation of underlying vascular risk, and new data suggest that CVD risk scores are more accurate in predicting CVD risk than the traditionally used age and years since menopause and should be incorporated into counseling. Finally, new data support the growing belief that breast arterial calcification on mammography is a promising noninvasive marker that can enhance CVD risk prediction in women.

**J Midlife Health. Jan-Mar 2022;13(1):80-84. doi: 10.4103/jmh.jmh\_150\_21. Epub 2022 May 2.**

### **Improvement in Quality of Life of Postmenopausal Women with Depression with commonly used Antidepressants (Escitalopram vs. Desvenlafaxine): A**

## Randomized Controlled Trial in a Tertiary Care Teaching Hospital of North India

Sonia Shinde Mahajan 1 2, Manu Arora 3, Vishal R Tandon 1, Annil Mahajan 4, Suman Kotwal 4

**Introduction:** The postmenopausal symptoms affect the quality of life (QoL) of women. Depression and anxiety too have been associated with diminished QoL. It is known that antidepressants escitalopram and desvenlafaxine are effective in the treatment of depression and anxiety. However, to the best of our knowledge, their comparative effect on the QoL of postmenopausal women with depression and anxiety has not been studied in the Indian setup. **Materials and methods:** The present study was a randomized, intention to treat, open-label trial undertaken in North India's a tertiary care teaching hospital. Postmenopausal women attending the psychiatry outpatient department and newly diagnosed with depression and anxiety were randomized in two groups to receive Tab. Escitalopram 10-20 mg and Tab. Desvenlafaxine 50-100 mg. Their QoL was assessed using the WHOQOL BREF scale at baseline, 3 weeks and 6 weeks. **Results:** Escitalopram was observed to be statistically better than desvenlafaxine in improving the overall QoL score of the WHOQOL-BREF scale. Individually, escitalopram significantly improved the scores of the physical health domain, psychological and environmental domains except for the social relationship domain. Desvenlafaxine significantly improved scores of all four domains. **Conclusion:** Escitalopram was observed to be significantly better than desvenlafaxine in improving the overall QoL scores. Both the drugs were well tolerated.

**Hum Reprod. 2022 Jun 12;deac137. doi: 10.1093/humrep/deac137. Online ahead of print.**

## Menopause, hysterectomy, menopausal hormone therapy and cause-specific mortality: cohort study of UK Biobank participants

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**Study question:** What is the association between menopausal hormone therapy (MHT) and cause-specific mortality?

**Summary answer:** Self-reported MHT use following early natural menopause, surgical menopause or premenopausal hysterectomy is associated with a lower risk of breast cancer mortality and is not consistently associated with the risk of mortality from cardiovascular disease or other causes. **What is known already:** Evidence from the Women's Health Initiative randomized controlled trials showed that the use of estrogen alone is not associated with the risk of cardiovascular mortality and is associated with a lower risk of breast cancer mortality, but evidence from the Million Women Study showed that use of estrogen alone is associated with a higher risk of breast cancer mortality. **Study design, size, duration:** Cohort study (the UK Biobank), 178 379 women, recruited in 2006-2010. **Participants/materials, setting, methods:** Postmenopausal women who had reported age at menopause (natural or surgical) or hysterectomy, and information on MHT and cause-specific mortality. Age at natural menopause, age at surgical menopause, age at hysterectomy and MHT were exposures of interest. Natural menopause was defined as spontaneous cessation of menstruation for 12 months with no previous hysterectomy or oophorectomy. Surgical menopause was defined as the removal of both ovaries prior to natural menopause. Hysterectomy was defined as removal of the uterus before natural menopause without bilateral oophorectomy. The study outcome was cause-specific mortality. **Main results and the role of chance:** Among the 178 379 women included, 136 790 had natural menopause, 17 569 had surgical menopause and 24 020 had hysterectomy alone. Compared with women with natural menopause at the age of 50-52 years, women with natural menopause before 40 years (hazard ratio (HR): 2.38, 95% CI: 1.64, 3.45) or hysterectomy before 40 years (HR: 1.60, 95% CI: 1.23, 2.07) had a higher risk of cardiovascular mortality but not cancer mortality. MHT use was associated with a lower risk of breast cancer mortality following surgical menopause before 45 years (HR: 0.17, 95% CI: 0.08, 0.36), at 45-49 years (HR: 0.15, 95% CI: 0.07, 0.35) or at  $\geq 50$  years (HR: 0.28, 95% CI: 0.13, 0.63), and the association between MHT use and the risk of breast cancer mortality did not differ by MHT use duration (<6 or 6-20 years). MHT use was also associated with a lower risk of breast cancer mortality following natural menopause before 45 years (HR: 0.59, 95% CI: 0.36, 0.95) or hysterectomy before 45 years (HR: 0.49, 95% CI: 0.32, 0.74). **Limitations, reasons for caution:** Self-reported data on age at natural menopause, age at surgical menopause, age at hysterectomy and MHT. **Wider implications of the findings:** The current international guidelines recommend women with early menopause to use MHT until the average age at menopause. Our findings support this recommendation.