



## Selección de Resúmenes de Menopausia

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### Evidence-based strategies to prevent cognitive decline in older people

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A helpful method to understand cognitive decline in older people is to consider this entity as increasing cognitive frailty caused by a number of interacting pathological processes. Over the last 20 years, multiple lifestyle, environmental and constitutional factors have been linked to the development of cognitive decline. For two interventions based on these factors, increasing physical activity and the control of hypertension, there is class 1 evidence for benefit. Other interventions based on these factors do not have the support of high-level evidence for the alteration of cognitive decline, but their other benefits would argue for their implementation. These interventions include increasing education, smoking cessation, avoiding head injuries, decreasing exposure to air pollution and increased social connections. As cognitive decline is experienced almost universally with ageing, and serious cognitive decline is experienced by substantial numbers of low-risk individuals, whole-of-population intervention strategies are the most effective and efficient. For other interventions to help prevent cognitive decline there is not sufficient evidence for their implementation to be recommended. These include alteration of alcohol ingestion, correction of hearing loss, treatment of depression, dietary interventions, menopausal hormone treatment and monoclonal antibodies directed against amyloid- $\beta$ .

**J Evid Based Med. 2024 Jun;17(2):377-389. doi: 10.1111/jebm.12622. Epub 2024 Jun 20.**

### Impact of hormone replacement therapy on all-cause and cancer-specific mortality in colorectal cancer: A systematic review and dose–response meta-analysis of observational studies

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**Objective:** The effect of hormone replacement therapy (HRT) on colorectal cancer (CRC) mortality and all-cause mortality remains unclear. We conducted a systematic review and dose-response meta-analysis to determine the effects of HRT on CRC mortality and all-cause mortality. **Methods:** We searched the electronic databases of PubMed, Embase, and The Cochrane Library for all relevant studies published until January 2024 to investigate the effects of HRT exposure on survival rates for patients with CRC. Two reviewers independently extracted individual study data and evaluated the risk of bias between the studies using the Newcastle–Ottawa Scale. We performed a two-stage random-effects dose-response meta-analysis to examine a possible nonlinear relationship between the year of HRT use and CRC mortality. **Results:** Ten cohort studies with 480,628 individuals were included. HRT was inversely associated with the risk of CRC mortality (hazard ratios (HR) = 0.77, 95% CI (0.68, 0.87), I<sup>2</sup> = 69.5%,  $p < 0.05$ ). The pooled results of seven cohort studies revealed a significant association between HRT and the risk of all-cause mortality (HR = 0.71, 95% CI (0.54, 0.92), I<sup>2</sup> = 89.6%,  $p < 0.05$ ). A linear dose-response analysis ( $p$  for nonlinearity = 0.34) showed a 3% decrease in the risk of CRC for each additional year of HRT use; this decrease was significant (HR = 0.97, 95% CI (0.94, 0.99),  $p < 0.05$ ). An additional linear ( $p$  for nonlinearity = 0.88) dose-response analysis showed a nonsignificant decrease in the risk of all-cause mortality for each additional year of HRT use. **Conclusions:** This study suggests that the use of HRT is inversely associated with all-cause and colorectal cancer mortality, thus causing a significant decrease in mortality rates over time. More studies are warranted to confirm this association.

**J Clin Med. 2024 Jun 17;13(12):3550. doi: 10.3390/jcm13123550.**

### The Efficacy of CO<sub>2</sub> Vaginal Laser in the Treatment of Recurrent, Post-Coital and Interstitial Cystitis: A Multicentric Prospective Study

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**Background:** This multicentric prospective study was carried out at Fondazione Policlinico Universitario Campus Bio Medico and Ospedale di Stato of St. Marino Republic. Between 1 January 2019, and 31 December 2022, all pre- and post-menopausal women diagnosed with recurrent, post-coital, and interstitial cystitis at both centers were included in

the study. The main aim of the study was to assess the effectiveness of vaginal CO<sub>2</sub> laser treatment, alone or combined with intravesical hyaluronic acid instillations, in managing cystitis symptoms, such as dysuria, pollakiuria, and urgency, across the entire patient cohort. The secondary objective was to investigate the reduction in number of annual cystitis episodes post-treatment. Methods: Each woman underwent three to four sessions of micro-ablative CO<sub>2</sub> vaginal laser treatment. A follow-up examination was conducted 12 months after the final laser session (up to December 2023), during which a post-treatment VAS assessment evaluated dysuria, daily pollakiuria, and urgency. The enrolled patients recorded the number of cystitis episodes experienced during the 12-month pre- and post-treatment period. Results: Results indicated the laser's efficacy in reducing the total number of cystitis episodes per year and an improvement in symptoms up to one year post-treatment. Greater efficacy of the CO<sub>2</sub> laser treatment, particularly when combined with intravesical hyaluronic acid instillation, was observed in both pre- and post-menopausal women. Conclusions: Fractional CO<sub>2</sub> laser therapy represents a safe and efficacious, non-hormonal approach for pre- and post-menopausal women diagnosed with recurrent, post-coital, and interstitial cystitis.

**Cancers (Basel). 2024 Jun 11;16(12):2197. doi: 10.3390/cancers16122197.**

### **Effects of Weight Loss on Key Obesity-Related Biomarkers Linked to the Risk of Endometrial Cancer: A Systematic Review and Meta-Analysis**

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Endometrial cancer (EC) includes various histologic types, with estrogen-dependent endometrioid carcinoma being the most common. Obesity significantly increases the risk of developing this type, especially in postmenopausal women, due to elevated estrogen production by adipocytes. This review examines the impact of weight loss from different interventions on reducing obesity-related risk factors for endometrioid EC. A systematic review and meta-analysis were conducted on three weight loss interventions: bariatric surgery, pharmacotherapy, and lifestyle changes. The effects of these interventions on inflammatory biomarkers (CRP, TNF- $\alpha$ , IL-6) and hormones (leptin, estrogen) were analyzed. Data from controlled studies were pooled to assess the significance of weight loss in reducing these biomarkers. Despite heterogeneity, bariatric surgery resulted in an overall 25.8% weight reduction, outperforming lifestyle and pharmacotherapy interventions. Weight loss reduced CRP levels by 33.5% and IL-6 levels by 41.9%. TNF- $\alpha$  levels decreased by 13% with percent weight loss over 7%. Leptin levels also decreased significantly, although the exact weight loss percentage was not statistically significant. Weight loss effectively reduces proinflammatory markers and hormones associated with increased risk of endometrioid EC. The strengths of this review include a comprehensive examination of different weight-loss interventions and a large pool of participants. However, limitations include high heterogeneity among studies and only 43% of the participants being postmenopausal. Limited data on sex hormones and racial disparities underscore the need for further research.

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### **The paradox of bone mineral density and fracture risk in type 2 diabetes**

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Fracture risk in type 2 diabetes (T2D) patients is paradoxically increased despite no decrease in areal bone mineral density (BMD). This phenomenon, known as the "diabetic bone paradox", has been attributed to various factors including alterations in bone microarchitecture and composition, hyperinsulinemia and hyperglycemia, advanced glycation end products (AGEs), and comorbidities associated with T2D. Zhao et al. recently investigated the relationship between T2D and fracture risk using both genetic and phenotypic datasets. Their findings suggest that genetically predicted T2D is associated with higher BMD and lower fracture risk, indicating that the bone paradox is not observed when confounding factors are controlled using Mendelian randomization (MR) analysis. However, in prospective phenotypic analysis, T2D remained associated with higher BMD and higher fracture risk, even after adjusting for confounding factors. Stratified analysis revealed that the bone paradox may disappear when T2D-related risk factors are eliminated. The study also highlighted the role of obesity in the relationship between T2D and fracture risk, with BMI mediating a significant portion of the protective effect. Overall, managing T2D-related risk factors may be crucial in preventing fracture risk in T2D patients.

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### **Female-specific risk factors for cardiovascular disease: an update**

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Cardiovascular disease (CVD) is the leading cause of morbidity and mortality worldwide. While it was previously believed that men have greater susceptibility to CVD, recent research suggests that women face an increased risk of CVD after the onset of menopause, primarily due to the loss of the protective effects of estrogens. Premature ovarian insufficiency (POI), polycystic ovarian syndrome (PCOS), and gestational factors, such as gestational diabetes mellitus (GDM), recurrent pregnancy loss, preterm delivery, and preeclampsia, are specific reproductive disorders that may contribute to an elevated risk of CVD at earlier ages, i.e., before the onset of menopause. This suggests that women with these conditions should be closely monitored for CVD risk factors even before reaching menopause. Such early intervention may help reduce the incidence of CVD and improve overall cardiovascular health in this population. The precise pathophysiological mechanism underlying the development of CVD in women with menopause, premature POI, PCOS, and gestational factors remains elusive. This review article seeks to elucidate the latest research on the relationship between these conditions and CVD in women, aiming to explore the underlying pathogenic mechanisms contributing to this association.

**Menopause. 2024 Jun 25. doi: 10.1097/GME.0000000000002386. Online ahead of print.**

### **Sleep disturbance associated with the menopause**

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**Importance and objectives:** Sleep disturbance is one of the most common and debilitating symptoms experienced by women during the menopause transition. However, there are currently no therapies specifically approved for sleep disturbance associated with the menopause. Here, we consider how to characterize sleep disturbance associated with the menopause and discuss its etiology, including the latest advances in our understanding of the neuronal circuits that regulate reproduction, body temperature, sleep, and mood; and reflect on its impact on women's health and well-being. **We also examine the current treatment landscape and look to the future of treatment for this condition. Methods:** We conducted a review of the literature and combined this with discussion with experts in the fields of sleep and menopause as well as experiences from our own clinical practices. **Discussion and conclusions:** Sleep disturbance associated with the menopause is characterized by frequent night-time awakenings and increased awake time after sleep onset. Its impacts are wide-ranging, negatively affecting health as well as personal and social relationships, productivity, and work performance. There is currently an unmet need for effective, safe, and well-tolerated treatments to address this important symptom, and wider recognition of the association between sleep disturbances and the menopause is needed. Sleep disturbances associated with the menopause can result from hormone changes as well as vasomotor and mood symptoms. Growing research has contributed to our knowledge of the role of hypothalamic estrogen-sensitive kisspeptin/neurokinin B/dynorphin neurons. These neurons are thought to integrate the gonadotropin-releasing hormone pathway and the pathways responsible for the homeostatic control of body temperature and the circadian regulation of sleep-wake cycles. Understanding these neurons offers the potential to create treatments that target a key cause of sleep disturbance associated with the menopause. Further research to understand their etiology and characterize the neuronal circuits responsible could benefit the development of these targeted treatment approaches.

**Br J Cancer. 2024 Jun 24. doi: 10.1038/s41416-024-02767-8. Online ahead of print.**

### **Hormone replacement therapy and cancer mortality in women with 17 site-specific cancers: a cohort study using linked medical records**

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**Background:** There is limited evidence on the safety of Hormone Replacement Therapy (HRT) in women with cancer. Therefore, we systematically examined HRT use and cancer-specific mortality in women with 17 site-specific cancers. **Methods:** Women newly diagnosed with 17 site-specific cancers from 1998 to 2019, were identified from general practitioner (GP) records, hospital diagnoses or cancer registries in Scotland, Wales and England. Breast cancer patients were excluded because HRT is contraindicated in breast cancer patients. The primary outcome was time to cancer-specific mortality. Time-dependent Cox regression models were used to calculate adjusted hazard ratios (HR) and 95% confidence intervals (95% CIs) for cancer-specific mortality by systemic HRT use. **Results:** The combined cancer cohorts contained 182,589 women across 17 cancer sites. Overall 7% of patients used systemic HRT after their cancer diagnosis. There was no evidence that HRT users, compared with non-users, had higher cancer-specific mortality at any cancer site. In particular, no increase was observed in common cancers including lung (adjusted HR = 0.98 95% CI 0.90, 1.07), colorectal (adjusted HR = 0.79 95% CI 0.70, 0.90), and melanoma (adjusted HR = 0.77 95% CI 0.58, 1.02). **Conclusions:** We observed no evidence of increased cancer-specific mortality in women with a range of cancers (excluding breast) receiving HRT.