



## Selección de Resúmenes de Menopausia

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### Progestogens for endometrial protection in combined menopausal hormone therapy: A systematic review

Petra Stute 1, Linus Josef Walker 2, Astrid Eicher 3, Elena Pavicic 4, Argyrios Kolokythas 5, Susanne Theis 6, et al. Menopausal women with an intact uterus choosing estrogens for menopausal symptom relief require a progestogen for endometrial protection. The aim of this systematic review was to evaluate the risks of endometrial hyperplasia resp. malignancy with different progestogens used in combined MHT. Overall, 84 RCTs were included. We found that 1) most studies were done with NETA, followed by MPA, MP and DYD and LNG, 2) most progestogens were only available as oral formulations, 3) the most frequently studied progestogens (oral MP, DYD, MPA, oral and transdermal NETA, transdermal LNG) were assessed in continuously as well as in sequentially combined MHT regimens, 4) FDA endometrial safety criteria were only fulfilled for some progestogen formulations, 5) most studies demonstrated endometrial protection for the progestogen dose and time period examined. However, 6) study quality varied which should be taken into account, when choosing a combined MHT, especially if off-label-use is chosen.

**Maturitas. 2023 Aug 18;177:107824. doi: 10.1016/j.maturitas.2023.107824. Online ahead of print.**

### Working well: Mitigating the impact of menopause in the workplace - A narrative evidence review

Nicola Dennis 1, Gemma Hobson 2

Introduction: In recent years there has been a much greater recognition by some employers of the need to support female employees experiencing the menopause. However, despite an increased awareness of the need to reduce the impact of menopause on the workforce, employers rarely have the opportunity to implement evidence-based interventions. Objectives: This evidence review aims to provide an insight into the effectiveness of workplace programmes supporting women experiencing menopause symptoms, and to identify knowledge gaps as drivers for future research. Methods: A search for papers published in English between 2012 and 2023 was carried out on the PsycINFO, Medline, and Embase databases. Abstract review was used to screen initial returns before a subsequent full-text review determined the final studies included. Results: Twelve studies were selected for in-depth review: four conducted in the UK, seven in continental Europe and one in South America. The findings of the papers fell into five categories: work ability, improved symptom management, mental wellbeing and empowerment, increased openness about menopause in the workplace, and the impact of management/leadership. None of the included interventions were reported to give a significant improvement in measures of work ability. However, there were improvements in women's wellbeing, and their ability to manage symptoms. Interventions to improve workplace openness and managers' skills were well received by participants. Conclusions: The evidence for effective workplace interventions for women experiencing menopause symptoms is currently lacking. There is considerable need for further high-quality evaluations of interventions designed to support women in the workplace.

**J Clin Med. 2023 Aug 12;12(16):5263. doi: 10.3390/jcm12165263.**

### Associations between Menopausal Hormone Therapy and Colorectal, Lung, or Melanoma Cancer Recurrence and Mortality: A Narrative Review

Gabriel Fiol 1, Iñaki Lete 1, Laura Nieto, Ana Santaballa, María Jesús Pla, Laura Baquedano, Joaquín Calaf, et al.

Objective: to develop eligibility criteria for use in non-gynecological cancer patients. Methods: We searched all the articles published in peer-reviewed journals up to March 2021. We utilized the PICOS standards and the following selection criteria: menopausal women with a history of non-gynecological and non-breast cancer who underwent hormone replacement therapy (HRT) using various preparations (oestrogens alone or in combination with a progestogen, tibolone, or tissue selective oestrogen complex) and different routes of administration (including oral, transdermal, vaginal, or intra-nasal). We focused on randomized controlled trials as well as relevant extension studies or follow-up reports, specifically examining recurrence and mortality outcomes. Results: Women colorectal cancer

survivors who use MHT have a lower risk of death from any cause than those survivors who do not use MHT. Women who are skin melanoma survivors using MHT have a longer survival rate than non-MHT survivors. There is no evidence that women lung cancer survivors who use MHT have a different survival rate than those who do not use MHT. Conclusions: MHT is safe for women who have a history of colorectal, lung, or skin melanoma cancers.

**Antioxidants (Basel). 2023 Aug 11;12(8):1601. doi: 10.3390/antiox12081601. Free**

## **The Role of Lifestyle and Dietary Factors in the Development of Premature Ovarian Insufficiency**

Andrew N Shelling 1 2, Noha Ahmed Nasef 3 4

Premature ovarian insufficiency (POI) is a **condition** that arises from dysfunction or early depletion of the ovarian follicle pool accompanied by an earlier-than-normal loss of fertility in young women. Oxidative stress has been suggested as an important factor in the decline of fertility in women and POI. In this review, we discuss the mechanisms of oxidative stress implicated in ovarian ageing and dysfunction in relation to POI, in particular mitochondrial dysfunction, apoptosis and inflammation. Genetic defects, autoimmunity and chemotherapy, are some of the reviewed hallmarks of POI that can lead to increased oxidative stress. Additionally, we highlight lifestyle factors, including diet, low energy availability and BMI, that can increase the risk of POI. The final section of this review discusses dietary factors associated with POI, including consumption of oily fish, mitochondria nutrient therapy, melatonin, dairy and vitamins that can be targeted as potential interventions, especially for at-risk women and in combination with personalised nutrition. Understanding the impact of lifestyle and its implications for POI and oxidative stress holds great promise in reducing the burden of this condition.

**Menopause. 2023 Sep 1;30(9):940-946. doi: 10.1097/GME.0000000000002230. Epub 2023 Aug 7.**

## **A phase 1/2, open-label, parallel group study to evaluate the preliminary efficacy and usability DARE-HRT1 (80 µg estradiol/4 mg progesterone and 160 µg estradiol/8 mg progesterone intravaginal RinGSM) over 12 weeks in healthy postmenopausal women**

Andrea Thurman 1, M Louise Hull 2, Bronwyn Stuckey 3, Jessica Hatheway 1, Nadene Zack, Christine Mauck, et al. Objectives: The exploratory objectives of this study were to evaluate the usability and acceptability and to conduct a preliminary evaluation of the efficacy of DARE-HRT1. DARE-HRT1 is an intravaginal ring (IVR) that releases 17β-estradiol (E2) with progesterone (P4) over 28 days. It is the first combination E2 and P4 IVR being developed for the treatment of vasomotor symptoms (VMS) in healthy postmenopausal women with an intact uterus. Methods: This was a randomized, open-label, 2-arm, parallel group study in 21 healthy postmenopausal women. Women were randomized (1:1) to either DARE-HRT1 IVR1 (E2 80 µg/d with P4 4 mg/d) or DARE-HRT1 IVR2 (E2 160 µg/d with P4 8 mg/d). They used the assigned IVR for three 28-day cycles, inserting a new IVR monthly. Preliminary genitourinary syndrome of menopause (GSM) treatment efficacy was estimated by measuring changes from baseline in vaginal pH, vaginal maturation index (VMI), and changes in the severity of GSM symptoms. Preliminary systemic VMS efficacy was measured by changes in responses to the Menopause-Specific Quality of Life (MENQOL) questionnaire. Acceptability was assessed by product experience surveys. Results: Preliminary local GSM treatment efficacy was supported by significant decreases in vaginal pH and % parabasal cells, and significant increases in the overall VMI and % superficial cells for both IVR groups (all P values <0.01). Preliminary VMS efficacy was supported by significant decreases in all domains of the MENQOL questionnaire from baseline for both dosing groups (all P values <0.01). Conclusions: Data from this study support further development of DARE-HRT1 for the treatment of menopausal symptoms.

**Menopause. 2023 Sep 1;30(9):887-897. doi: 10.1097/GME.0000000000002237.**

## **Association of menopausal vasomotor symptom severity with sleep and work impairments: a US survey**

Barbara DePree 1, Aki Shiozawa 2, Deanna King, Arianne Schild, Mo Zhou, Hongbo Yang, Shayna Mancuso.

Objective: Menopausal vasomotor symptoms commonly disrupt sleep and affect daytime productivity. This online survey evaluated associations between vasomotor symptom severity and perceived sleep quality and work productivity.

Methods: Participants were perimenopausal or postmenopausal US women aged 40 to 65 years with  $\geq 14$  vasomotor symptom episodes per week for  $\geq 1$  week in the past month. The women, who were recruited from Dynata panels via email invitation and categorized by vasomotor symptom severity based on the Menopause Rating Scale, were surveyed about sleep and work productivity and completed the Patient-Reported Outcomes Measurement Information System Sleep Disturbance Short Form 8b (primary outcome) and Sleep-Related Impairment Short Form 8a, Pittsburgh Sleep Quality Index, and Work Productivity and Activity Impairment questionnaire. Results: Among 619 respondents (mean age, 53 y; White, 91%; perimenopausal, 34%; postmenopausal, 66%; 57.5% were never treated for vasomotor symptoms), vasomotor symptoms were mild in 88, moderate in 266, and severe in 265. A majority (58% overall) were employed, including 64.8%, 49.6%, and 64.2% of women with mild, moderate, and severe VMS, respectively. Of the 90.8% who reported that vasomotor symptoms affect sleep (81.8%, 86.8%, and 97.7% of those with mild, moderate, and severe VMS), 83.1% reported sleep-related changes in productivity (75.0%, 73.2%, and 94.2%, respectively). Patient-Reported Outcomes Measurement Information System Sleep Disturbance Short Form 8b mean T scores in the mild (T score, 53.5), moderate (57.3), and severe (59.8) VMS cohorts indicated more sleep disturbance than in the general population (T score, 50; overall  $P < 0.001$  before and after controlling for confounding variables). Sleep-Related Impairment 8a results were similar. Vasomotor symptom severity was positively associated with Pittsburgh Sleep Quality Index mean scores, presenteeism, absenteeism, overall work impairment, and impairment in general activities. Conclusions: Greater vasomotor symptom severity was associated with more sleep disturbance, more sleep-related impairment, worse sleep quality, and greater impairment in daytime activities and work productivity.

**Cochrane Database Syst Rev. 2023 Aug 24;8(8):CD009672. doi: 10.1002/14651858.CD009672.pub3.**

## **Hormone therapy for sexual function in perimenopausal and postmenopausal women**

Lucia A Lara 1, Denisse Cartagena-Ramos 2, Jaqueline Bp Figueiredo 1 3, Ana Carolina Js Rosa-E-Silva 1, et al.

Objectives: We aimed to assess the effect of hormone therapy on sexual function in perimenopausal and postmenopausal women. Search methods: On 19 December 2022 we searched the Gynaecology and Fertility Group Specialised Register, CENTRAL, MEDLINE, Embase, PsycINFO, CINAHL, LILACS, ISI Web of Science, two trials registries, and OpenGrey, together with reference checking and contact with experts in the field for any additional studies. Main results: We included 36 studies (23,299 women; 12,225 intervention group; 11,074 control group), of which 35 evaluated postmenopausal women; only one study evaluated perimenopausal women. Authors' conclusions: Hormone therapy treatment with estrogen alone probably slightly improves the sexual function composite score in women with menopausal symptoms or in early postmenopause (within five years of amenorrhoea), and in unselected postmenopausal women, especially in the lubrication, pain, and satisfaction domains. We are uncertain whether estrogen combined with progestogens improves the sexual function composite score in unselected postmenopausal women. Evidence regarding other hormone therapies (synthetic steroids and SERMs) is of very low quality and we are uncertain of their effect on sexual function. The current evidence does not suggest the beneficial effects of synthetic steroids (for example tibolone) or SERMs alone or combined with estrogen on sexual function. More studies that evaluate the effect of estrogen combined with progestogens, synthetic steroids, SERMs, and SERMs combined with estrogen would improve the quality of the evidence for the effect of these treatments on sexual function in perimenopausal and postmenopausal women.