

# Menopause

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## 1. Efficacy and safety of fezolinetant for vasomotor symptoms in postmenopausal women: A systematic review and meta-analysis of randomized controlled trials

**Authors:** Akhtar, Syed Muhammad Muneeb;Ali, Abraish;Khan, Muhammad Sohaib;Khan, Vareesha;Fareed, Areeba;Saleem, Syed Zia;Mumtaz, Munazza;Ahsan, Muhammad Nadeem;Iqbal, Sadia and Asghar, Muhammad Sohaib

**Publication Date:** 2024

**Journal:** International Journal of Gynaecology & Obstetrics

**Abstract:** **BACKGROUND:** Vasomotor symptoms (VMS), such as hot flashes and night sweats, are highly prevalent and burdensome for women experiencing menopausal transition. Fezolinetant, a selective neurokinin 3 receptor (NK3R) antagonist, is a potential therapeutic option for mitigating VMS. **OBJECTIVES:** Our aim is to assess the efficacy and evaluate the safety profile of fezolinetant compared with placebo in post-menopausal women suffering from VMS, by pooling all the relevant data and reflecting the most current evidence. **SEARCH STRATEGY/SELECTION CRITERIA:** An extensive literature search was performed in the PubMed, Medline and Cochrane Library databases from inception until June 2023 to identify relevant trials. **DATA COLLECTION AND ANALYSIS:** Mean differences (MDs) and 95% confidence intervals (CIs) were calculated for continuous outcomes. Risk ratios (RRs) were calculated for dichotomous outcomes. All statistical analyses were performed using R Statistical Software. **MAIN RESULTS:** A total of six randomized controlled trials were added. For the frequency of daily VMS, the combined pooled result favored the fezolinetant group over placebo (MD -2.38, 95% CI -2.64 to -2.12;  $P = 0\%$ ). For the severity of daily VMS, fezolinetant was again found to be superior to the placebo group (MD -0.40, 95% CI -0.51 to -0.29;  $P = 0\%$ ). For the severity of daily VMS, fezolinetant was again found to be superior to the placebo group (MD -0.40, 95% CI -0.51 to -0.29;  $P = 70\%$ ). Fezolinetant (120 mg) consistently demonstrated a significant reduction in the severity of daily moderate/severe VMS compared with other doses at both 4 and 12 weeks. Patient-reported outcomes (PROs) of Greene Climacteric Scale (GCS), PROMIS the Sleep Disturbance Short Form 8b and Menopause-Specific Quality of Life (MENQoL) scores indicated significant improvement with fezolinetant. No significant difference in efficacy of fezolinetant at 4 and 12 weeks were observed in any outcome. As for safety, no significant differences in the treatment emergent adverse events at 12 weeks were found between fezolinetant and placebo. **CONCLUSIONS:** Our study significantly favors fezolinetant over placebo regarding the primary efficacy outcomes of daily moderate to severe VMS frequency and severity, including PROs, while both the groups are comparable in terms of treatment emergent adverse events. Further studies are needed to confirm these findings. Copyright © 2024 International Federation of Gynecology and Obstetrics.

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## 2. The association of vasomotor symptoms with fracture risk and bone mineral density in postmenopausal women: a systematic review and meta-analysis of observational studies

**Authors:** Anagnostis, Panagiotis;Lallas, Konstantinos;Pappa, Anna;Avgeris, Georgios;Beta, Kristina;Damakis, Dimitrios;Fountoukidou, Eirini;Zidrou, Maria;Lambrinouadaki, Irene and Goulis, Dimitrios G.

**Publication Date:** 2024

**Journal:** Osteoporosis International

**Abstract:** **BACKGROUND/AIMS:** Vasomotor symptoms (VMS) adversely affect postmenopausal quality of life. However, their association with bone health has not been elucidated. This study aimed to systematically review and meta-analyze the evidence regarding the association of VMS with fracture risk and bone mineral density (BMD) in peri- and postmenopausal women. **METHODS:** A literature search was conducted in PubMed, Scopus and Cochrane databases until 31 August 2023. Fracture,

low BMD (osteoporosis/osteopenia) and mean change in lumbar spine (LS) and femoral neck (FN) BMD were assessed. The results are presented as odds ratio (OR) and mean difference (MD), respectively, with a 95% confidence interval (95% CI). The  $I^2$  index quantified heterogeneity. **RESULTS:** Twenty studies were included in the qualitative and 12 in the quantitative analysis ( $n=49,659$ ). No difference in fractures between women with and without VMS was found ( $n=5$ , OR 1.04, 95% CI 0.93-1.16,  $I^2$  16%). However, VMS were associated with low BMD ( $n=5$ , OR 1.54, 95% CI 1.42-1.67,  $I^2$  0%). This difference was evident for LS (MD -0.019 g/cm<sup>2</sup>, 95% CI -0.03 to -0.008,  $I^2$  85.2%), but not for FN BMD (MD -0.010 g/cm<sup>2</sup>, 95% CI -0.021 to 0.001,  $I^2$  78.2%). These results were independent of VMS severity, age and study design. When the analysis was confined to studies that excluded menopausal hormone therapy use, the association with BMD remained significant. **CONCLUSIONS:** The presence of VMS is associated with low BMD in postmenopausal women, although it does not seem to increase fracture risk. Copyright © 2024. The Author(s).

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### 3. Systematic review and meta-analysis of the effects of menopause hormone therapy on cognition.

**Authors:** Andy, C.;Nerattini, M.;Jett, S.;Carlton, C.;Zarate, C.;Boneu, C.;Fauci, F.;Ajila, T.;Battista, M.;Pahlajani, S.;Christos, P.;Fink, M. E.;Williams, S.;Brinton, R. D. and Mosconi, L.

**Publication Date:** 2024

**Journal:** Frontiers in Endocrinology 15, Article Number: 1350318.

**Abstract:** Despite evidence from preclinical studies suggesting estrogen's neuroprotective effects, the use of menopausal hormone therapy (MHT) to support cognitive function remains controversial.

**Methods:** We used random-effect meta-analysis and multi-level meta-regression to derive pooled standardized mean difference (SMD) and 95% confidence intervals (C.I.) from 34 randomized controlled trials, including 14,914 treated and 12,679 placebo participants.

**Results:** Associations between MHT and cognitive function in some domains and tests of interest varied by formulation and treatment timing. While MHT had no overall effects on cognitive domain scores, treatment for surgical menopause, mostly estrogen-only therapy, improved global cognition (SMD=1.575, 95% CI 0.228, 2.921;  $P=0.043$ ) compared to placebo. When initiated specifically in midlife or close to menopause onset, estrogen therapy was associated with improved verbal memory (SMD=0.394, 95% CI 0.014, 0.774;  $P=0.046$ ), while late-life initiation had no effects. Overall, estrogen-progestogen therapy for spontaneous menopause was associated with a decline in Mini Mental State Exam (MMSE) scores as compared to placebo, with most studies administering treatment in a late-life population (SMD=-1.853, 95% CI -2.974, -0.733;  $P=0.030$ ). In analysis of timing of initiation, estrogen-progestogen therapy had no significant effects in midlife but was associated with improved verbal memory in late-life ( $P=0.049$ ). Duration of treatment >1 year was associated with worsening in visual memory as compared to shorter duration. Analysis of individual cognitive tests yielded more variable results of positive and negative effects associated with MHT.

**Discussion:** These findings suggest time-dependent effects of MHT on certain aspects of cognition, with variations based on formulation and timing of initiation, underscoring the need for further research with larger samples and more homogeneous study designs.

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### 4. The effect of resistance training in reducing hot flushes in post-menopausal women: A meta-analysis.

**Authors:** Choudhry, D. N.;Saleem, S.;Hatim, S. and Irfan, R.

**Publication Date:** 2024

**Journal:** Journal of Bodywork and Movement Therapies 39, pp. 335-342

**Abstract:** Objective: The objective of this meta-analysis is to study the effect of different strengths of

resistance training programs on the severity and frequency of hot flushes in postmenopausal women with vasomotor symptoms.

**Materials and methods:** Online research was conducted through databases such as PubMed, Cochrane Trial Register, and Google Scholar till the 20th of March 2023. The Review Manager (version 5.4.1) was used to statistically analyze the data from the studies. Studies meeting the inclusion criteria, comparing the vasomotor symptoms in resistance training groups as compared to control were used for this meta-analysis. The primary outcome of interest was the alleviation of hot flushes in the resistance training group. Random-effect model was used to pool the studies and the result was reported in SMD with 95% Confidence Interval (CI).

**Results:** 5 studies were selected for this review. Statistical analysis shows that vasomotor symptoms were more common in the control group and decreased significantly in the resistance training group after the intervention (SMD = -1.31, 95% CI: -1.85 to -0.77, p = 0.002).

**Conclusion:** Resistance Training significantly affects vasomotor symptoms and can be considered for such symptoms in postmenopausal women.

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## 5. "Not feeling like myself" in perimenopause - what does it mean? Observations from the Women Living Better survey.

**Authors:** Coslov, Nina;Richardson, Marcie K. and Woods, Nancy Fugate

**Publication Date:** 2024

**Journal:** Menopause

**Abstract: OBJECTIVE:** This study aimed to understand the meaning of the phrase "not feeling like myself" (NFLM) when used by those on the path to menopause by exploring the relationship of symptoms reported to ratings of NFLM. **METHODS:** Participants responded to the item "Many women report just not feeling like themselves during this phase of life. How often was this true for you over the past 3 months?" choosing from "none of the time" to "all of the time." They rated bother associated with 61 symptoms and provided demographic information. Individual symptoms and the symptom bother scale scores were correlated with NFLM. Symptom scale scores were then entered in a two-stage multiple regression model to identify symptoms associated significantly with NFLM. **RESULTS:** Sixty-three percent (63.3%) of participants reported NFLM 50% of the time or more over the previous 3 months. Individual symptom ratings correlated with NFLM ( $r > 0.300$ ) included the following: fatigue ( $r = 0.491$ ); feeling overwhelmed/less able to cope ( $r = 0.463$ ); low feelings ( $r = 0.440$ ); anxiety, more nervousness ( $r = 0.398$ ); being irritable ( $r = 0.380$ ); harder time concentrating ( $r = 0.378$ ); difficulty making decisions ( $r = 0.357$ ); feeling like "I can't calm down on the inside" ( $r = 0.333$ ); being more forgetful ( $r = 0.332$ ); tearfulness/crying ( $r = 0.306$ ); and worrying more ( $r = 0.302$ ). A two-stage regression analysis revealed less education completed and greater overall stress ratings as significant predictors in stage 1. In stage 2, five symptom groups met the P : Sixty-three percent (63.3%) of participants reported NFLM 50% of the time or more over the previous 3 months. Individual symptom ratings correlated with NFLM ( $r > 0.300$ ) included the following: fatigue ( $r = 0.491$ ); feeling overwhelmed/less able to cope ( $r = 0.463$ ); low feelings ( $r = 0.440$ ); anxiety, more nervousness ( $r = 0.398$ ); being irritable ( $r = 0.380$ ); harder time concentrating ( $r = 0.378$ ); difficulty making decisions ( $r = 0.357$ ); feeling like "I can't calm down on the inside" ( $r = 0.333$ ); being more forgetful ( $r = 0.332$ ); tearfulness/crying ( $r = 0.306$ ); and worrying more ( $r = 0.302$ ). A two-stage regression analysis revealed less education completed and greater overall stress ratings as significant predictors in stage 1. In stage 2, five symptom groups met the P **CONCLUSIONS:** NFLM was associated with anxiety/vigilance, fatigue/pain, brain fog, sexual symptoms, and volatile mood symptoms. Recognizing symptoms associated with NFLM may allow for more accurate expectations and improve perimenopause care. Copyright © 2024 The Author(s). Published by Wolters Kluwer Health, Inc. on behalf of The Menopause Society.

## 6. Prediagnostic use of menopausal hormone therapy and long-term survival of localized epithelial ovarian cancer: The Extreme study.

**Authors:** Duus, Alberte Hjorth;Hannibal, Charlotte Gerd;Baandrup, Louise;Zheng, Guoqiao;Galanakis, Michael;Maltesen, Thomas;Hertzum-Larsen, Rasmus;Morch, Lina S. and Kjaer, Susanne K.

**Publication Date:** 2024

**Journal:** International Journal of Cancer

**Abstract:** Use of menopausal hormone therapy (MHT) prior to an epithelial ovarian cancer (EOC) diagnosis has been suggested to be associated with improved survival. In a recent nationwide cohort study, we found that prediagnostic long-term MHT use, especially estrogen therapy (ET), was associated with improved long-term survival in women with nonlocalized EOC. Our aim was to investigate the influence of prediagnostic MHT use on long-term survival among women with localized EOC in the same nationwide study. Our study cohort comprised all women aged 50 years or older with an EOC diagnosis in Denmark 2000-2014 (n = 2097) identified from the Extreme study. We collected information on usage of systemic ET and estrogen plus progestin therapy (EPT) from the Danish National Prescription Registry. By using pseudo-values, 5- and 10-year absolute and relative survival probabilities were estimated with 95% confidence intervals (CIs) while adjusting for histology, comorbidity, and income. Relative survival probabilities >1 indicate better survival. The 5-year absolute survival probabilities were 61% and 56%, respectively, among women who were nonusers and users of prediagnostic MHT, whereas these numbers were 46% and 41%, respectively, regarding 10-year survival. Use of MHT was not significantly associated with an improved 5- or 10-year survival in women with localized EOC (5-year relative survival probability = 0.95, 95% CI: 0.89-1.02; 10-year relative survival probability = 0.92, 95% CI: 0.84-1.02). Similar findings were seen for systemic ET or EPT use. Our findings do not suggest a positive benefit from prediagnostic MHT use on long-term survival of localized EOC. Copyright © 2024 UICC.

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## 7. Effect of Hormone Replacement Therapy on Chronic Rhinosinusitis Management.

**Authors:** Herrera, Kevin;Parikh, Miti;Vemula, Sahiti and Hur, Kevin

**Publication Date:** 2024

**Journal:** Laryngoscope

**Abstract: OBJECTIVES:** To investigate whether hormone replacement therapy (HRT) impacts health care resource utilization in the management of chronic rhinosinusitis (CRS) in older women. **METHODS:** Using the TriNetX US health record database, women 55 years or older with a diagnosis of CRS were included and followed for 3 years. The cohort was stratified into two groups: women who received HRT at the beginning of the study were compared to women who did not receive HRT. The groups were matched by age, race, ethnicity, history of asthma, and history of nasal polyps. Outcomes included whether the patient underwent endoscopic sinus surgery (ESS) and frequency of antibiotic use. Measures of association, Kaplan-Meier analysis, and cohort descriptive statistics were calculated. **RESULTS:** Of the 65,400 women included, the mean age was 66.9 years. 27.0% and 3.6% of patients had a history of asthma or nasal polyps, respectively. Overall, 2.0% of CRS patients underwent ESS, with the HRT group less likely to undergo ESS [OR: 0.28; 95% CI: (0.25-0.32)] compared to patients who did not receive HRT. When stratified by polyp status, HRT patients with nasal polyps had a greater decrease in ESS rates compared to control than HRT patients without nasal polyps. The HRT group had a higher mean number of antibiotic prescriptions compared to the non-HRT group. **CONCLUSION:** HRT is associated with decreased utilization of ESS to treat CRS, with a greater effect size for ESS among CRSwNP patients. However, HRT was associated with higher antibiotic utilization. **LEVEL OF EVIDENCE:** Level 3 Laryngoscope, 2024. Copyright © 2024 The Authors. The Laryngoscope published by Wiley Periodicals LLC on behalf of The American Laryngological, Rhinological and Otological Society, Inc.

## 8. An empowerment model for managing menopause.

**Authors:** Hickey, M.;LaCroix, A. Z.;Doust, J.;Mishra, G. D.;Sivakami, M.;Garlick, D. and Hunter, M. S.

**Publication Date:** 2024

**Journal:** The Lancet 403(10430), pp. 947-957

**Abstract:** Menopause eventually happens to all people with typically functioning ovaries, and almost one billion women worldwide are postmenopausal. Although the biology of typical menopause is ubiquitous, the experience varies substantially. Factors contributing to the experience include not only individual factors, such as the nature and severity of symptoms, but also psychological, social, and contextual considerations, many of which are modifiable. In this first paper in the Lancet Series on menopause, we argue for a new approach that goes beyond the treatment of specific symptoms, to encompass a broad model to support women transitioning this life stage, using the model of empowerment. WHO defines empowerment as an active process of gaining knowledge, confidence, and self-determination to self-manage health and make informed decisions about care. Rather than focusing on menopause as an endocrine deficiency, we propose an empowerment model that recognises factors modifying the experience, in which the patient is an expert in their own condition and the health-care worker supports the patient to become an equal and active partner in managing their own care.

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## 9. A Cost Savings Analysis of Topical Estrogen Therapy in Urinary Tract Infection Prevention Among Postmenopausal Women.

**Authors:** Houston, C. G.;Azar, W. S.;Huang, S. S.;Rubin, R.;Dorris, C. S. and Sussman, R. D.

**Publication Date:** 2024

**Journal:** Urology Practice 11(2), pp. 257-266

**Abstract:** Introduction: UTIs are some of the most common infections in geriatric patients, with many women experiencing recurrent infections after menopause. In the US, annual UTI-related costs are \$2 billion, with recurrent infections creating a significant economic burden. Given the data published on topical estrogen in reducing the number of infections for postmenopausal women with recurrent UTI, we sought to evaluate how this would translate to cost savings.

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## 10. Hormone replacement therapy and periodontitis progression in postmenopausal women: A prospective cohort study.

**Authors:** Man, Ying;Zhang, Cui;Cheng, Cheng;Yan, Laiqi;Zong, Min and Niu, Feifei

**Publication Date:** 2024

**Journal:** Journal of Periodontal Research

**Abstract:** **OBJECTIVE:** This study aimed to investigate the responses of periodontal environment to hormone replacement therapy (HRT) in postmenopausal women with or without periodontitis. **BACKGROUND:** HRT is a common and effective strategy for controlling menopausal symptoms, while the changes of periodontal environment under it, particularly in postmenopausal women with periodontitis, remain unclear. **METHODS:** As a prospective cohort study, a total of 97 postmenopausal women receiving HRT were screened, including 47 with and 50 without periodontitis. Correspondingly, 97 women did not receiving HRT were screened as controls during the same period. The full-mouth sulcus bleeding index (SBI), bleeding on probing (BOP), probing pocket depth (PPD), and clinical attachment level (CAL) were measured using periodontal probes. The levels of interleukin-6 (IL-6) and tumor necrosis factor alpha (TNF-alpha) in the gingival crevicular fluid were measured

using enzyme-linked immunosorbent assay. In addition, cone beam computed tomography was performed to measure the alveolar bone height (ABH) and bone mineral density (BMD). **RESULTS:** In postmenopausal women without periodontitis, no significant changes on periodontal parameters were observed after HRT. In women with stage II periodontitis, SBI, BOP, IL-6, and TNF-alpha were significantly decreased after one year and two years of HRT. Compared to the controls, women with stage II periodontitis who underwent HRT had significantly lower CAL and ABH and higher BMD in the second year. The incidence of at least one site with CAL increase  $\geq 1$  mm between baseline and 2 years was significantly lower in the HRT group than in the control group in women with stage II periodontitis. In addition, HRT was significantly associated with a decrease in SBI, BOP, IL-6, and TNF-alpha in the first year and with a decrease in CAL, SBI, BOP, IL-6, and ABH and an increase in BMD in the second year. **CONCLUSIONS:** In postmenopausal women with stage II periodontitis, HRT is associated with the alleviation of inflammation within two years and the remission of alveolar bone loss in the second year. HRT appears to decrease the incidence of CAL increase  $\geq 1$  mm within 2 years in women with periodontitis by inhibiting inflammation and alveolar bone loss. Copyright © 2024 John Wiley & Sons A/S. Published by John Wiley & Sons Ltd.

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### 11. Association of age at menarche, reproductive lifespan and age at menopause with the risk of atrial fibrillation: The HUNT study.

**Authors:** Morooka, Hikaru;Haug, Eirin B.;Malmo, Vegard;Loennechen, Jan Pal;Mukamal, Kenneth J.;Rich-Edwards, Janet;Sen, Abhijit;Janszky, Imre and Horn, Julie

**Publication Date:** Mar 26 ,2024

**Journal:** Maturitas 185

**Abstract: BACKGROUND:** Age at menarche, reproductive lifespan, and age at menopause are associated with several cardiovascular diseases, but their relationship with atrial fibrillation (AF) is uncertain. **METHODS:** We linked information on all women who participated in the third survey of the population-based, longitudinal HUNT study in Norway with medical records from all local hospitals. A total of 14,632 women aged 60 or more were followed for validated incident AF. We retrieved age at menarche and age at menopause from the HUNT questionnaires. Reproductive lifespan was defined as the difference between age at menarche and age at menopause. We used Cox proportional hazards regression models to assess associations between AF and age at menarche, reproductive lifespan, and age at menopause. **RESULTS:** During a median follow-up of 8.17 years (136,494 person-years), 1217 (8.3 %) participants developed AF. In multivariable-adjusted analyses, we observed no associations between early or late age at menarche and AF (hazard ratios (HRs):  $\geq 16$  years: 0.99 [95 % CI, 0.80-1.24] compared to those who attained menarche at 13-14 years). The HR for a reproductive lifespan shorter than 30 years was 0.91 [95 % CI, 0.72-1.15] compared to 34-37 years. Likewise, there was no clear association between premature or early age at menopause and AF (HRs:  $\geq 16$  years: 0.99 [95 % CI, 0.80-1.24] compared to those who attained menarche at 13-14 years). The HR for a reproductive lifespan shorter than 30 years was 0.91 [95 % CI, 0.72-1.15] compared to 34-37 years. Likewise, there was no clear association between premature or early age at menopause and AF (HRs: **CONCLUSIONS:** In this population of women aged 60 years and over, the risk of AF was not associated with age at menarche, reproductive lifespan, or age at menopause. Copyright © 2024. Published by Elsevier B.V.

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### 12. Design of OASIS 1 and 2: phase 3 clinical trials assessing the efficacy and safety of elinzanetant for the treatment of vasomotor symptoms associated with menopause.

**Authors:** Pinkerton, JoAnn V.;Simon, James;Panay, Nick;Seitz, Christian;Parke, Susanne;Caetano, Cecilia;Mellinger, Uwe;Haseli Mashhadi, Nazanin;Haberland, Claudia;Atanackovic, Gordana;Holz, Cornelia;Mao, Guangping;Morrison, Marina;Nisius, Sven;Schaefer, Matthias and Zuurman, Lineke

**Publication Date:** 2024

**Journal:** Menopause

**Abstract: OBJECTIVE:** Elinzanetant is a selective neurokinin-1,3 receptor antagonist in development for the treatment of vasomotor symptoms (VMS) associated with menopause. The pivotal, double-blind, randomized, placebo-controlled phase 3 studies Overall Assessment of efficacy and Safety of elinzanetant In patients with vasomotor Symptoms (OASIS) 1 and 2 will assess the efficacy and safety of elinzanetant in women with VMS. **METHODS:** The OASIS 1 and 2 pivotal studies are designed in accordance with regulatory guidance. Postmenopausal women with moderate/severe VMS are randomized to receive 120 mg elinzanetant or placebo once daily for 12 weeks, followed by a 14-week active treatment extension. Primary endpoints are the mean change in frequency and severity of moderate/severe VMS from baseline to weeks 4 and 12. Key secondary endpoints will assess the onset of action and effects on sleep disturbance and menopause-related quality of life. Primary and key secondary endpoints will be analyzed using a mixed model with repeated measures. Feedback from postmenopausal women with VMS was used during protocol development. **RESULTS:** Women confirmed the relevance of endpoints that assess the impact of VMS, sleep disturbance, and mood changes, and the need for new nonhormone treatments. Educational materials around study design, conduct and expected assessments and procedures were developed based on questions and concerns raised by women. **CONCLUSIONS:** The OASIS 1 and 2 pivotal phase 3 studies will enable assessment of the efficacy and safety of elinzanetant as a treatment for VMS, together with its effect on sleep disturbances, depressive symptoms, and menopause-related quality of life. Feedback from postmenopausal women with VMS was used to maximize patient centricity in the trials. Copyright © 2024 The Author(s). Published by Wolters Kluwer Health, Inc. on behalf of The Menopause Society.

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### 13. Follicle-Stimulating Hormone and Diabetes in Postmenopausal Women: A Systematic Review and Meta-analysis.

**Authors:** Saei Ghare Naz, Marzieh;Farhadi-Azar, Mahbanoo;Noroozadeh, Mahsa;Farahmand, Maryam and Ramezani Tehrani, Fahimeh

**Publication Date:** 2024

**Journal:** Journal of Clinical Endocrinology & Metabolism

**Abstract: BACKGROUND:** Today, co-occurrence of hormonal changes during menopause and the risk of cardio-metabolic disorders have been well studied. We aimed to explore the association of circulating levels of follicle-stimulating hormone (FSH) with diabetes (DM) among postmenopausal women. **METHOD:** In this Systematic review and meta-analysis the search was performed on PubMed, Scopus, Web of sciences, Epistemonikos, and Cochrane library until the September 2023. Risk of bias was assessed by Newcastle-Ottawa Quality Assessment Scale. Pooled estimates of mean differences in FSH levels among diabetic postmenopausal women compared to those without diabetes were performed. Also, the correlation between FSH and fasting blood glucose (FBG)/Insulin/Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) as well as the pooled effect sizes with their 95% confidence intervals (CIs) for risk of DM were calculated. **RESULTS:** In this study, 14 articles, including 7,878 postmenopausal women, met eligibility criteria and were further analyzed. Most of the included studies had a low/moderate risk of bias. Women with DM had significantly lower FSH levels than those without DM (standardized mean difference [95% CI] -0.751, 95% CI-1.129 to -0.372, I2 = 82.46%, n = 1416). The pooled effect size (ES) for diabetes was 0.861 (95% CI: 0.740-1.001; I2 = 80.11%). The pooled risk estimate for DM based on the categorical FSH levels (high versus low) was (HR = 0.550; 95% CI, 0.356 to 0.850, I2 = 0). The significant inverse correlation was found between FSH levels and glycemic parameters [FBG (r= -0.285; 95%CI -0.441 to -0.113; n = 1229), HOMA-IR (r = -0.241; 95%CI -0.378 to -0.0924; n = 1229) and Insulin (r = -0.337; 95%CI -0.434 to -0.232; n = 959)]. There were no statistically significant differences between estradiol levels among diabetic and non-diabetic groups; however the SMD for luteinizing hormone was similar to that reported for FSH. **CONCLUSION:** The available data indicated an indirect association between FSH levels and glucose disturbances among postmenopausal women; notwithstanding heterogeneity among included studies, and the complexity of



various influential factors needs to be considered. Further efforts should be made to clarify the underlying mechanisms. Copyright © The Author(s) 2024.

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#### 14. The effectiveness of psychosocial interventions on non-physiological symptoms of menopause: A systematic review and meta-analysis.

**Authors:** Spector, A.;Li, Z.;He, L.;Badawy, Y. and Desai, R.

**Publication Date:** 2024

**Journal:** Journal of Affective Disorders 352, pp. 460-472

**Abstract:** Background: Menopause, a crucial transitioning stage for women, can significantly impact mood and wellbeing. We aimed to evaluate the effectiveness of psychosocial interventions on non-physiological symptoms of menopause (depression, anxiety, cognition, and quality of life) through systematic review and meta-analysis. Methods: Five databases were searched from inception to August 2023 for randomized controlled trials. Pre- and post-test means and standard deviations for groups were extracted and used to calculate effect sizes. The effectiveness of Cognitive Behavioral Therapy (CBT) and Mindfulness-Based Interventions (MBI) on depression and anxiety were examined by subgroup analysis.

Results: Thirty studies comprising 3501 women were included. From meta-analysis, mood symptoms significantly benefited from CBT (anxiety:  $d = -0.22$ , 95 % CI = -0.35, -0.10; depression:  $d = -0.33$ , 95 % CI = -0.45, -0.21) and MBI (anxiety:  $d = -0.56$ , 95 % CI = -0.74, -0.39; depression:  $d = -0.27$ , 95 % CI = -0.45, -0.09). Psychosocial interventions were also found to significantly improve cognition ( $d = -0.23$ , 95 % CI = -0.40, -0.06) and quality of life ( $d = -0.78$ , 95 % CI = -0.93, -0.63). Mean total therapy hours ('dose') was lower for CBT (11.3) than MBI (18.6), indicating reduced costs and burden for women.

Limitations: Data regarding menopausal status were not collected, limiting our ability to identify the optimal timing of interventions. Potential longer-term, effects of interventions were not investigated.

Conclusion: Our review highlighted the value of psychosocial interventions in improving non-physiological symptoms (particularly depression and anxiety) during menopause, noting the heterogeneity of findings and importance of implementing effective interventions.

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#### 15. A retrospective audit of general practitioner's referrals to Guys and St Thomas' specialist menopause clinic between 2021 and 2022.

**Authors:** Tedajo Tsambou, Jocelyne;Bruce, Deborah;Holloway, Debra and Rymer, Janice

**Publication Date:** Mar 21 ,2024

**Journal:** Post Reproductive Health

**Abstract: Purpose:** We performed a retrospective audit of General Practitioners' (GPs) referrals to the specialist Menopause Clinic at Guys and St Thomas's (GSTT) between 2021 and 2022. We aim to establish the indication for the referrals and whether they were compliant with the National Institute for Health and Care Excellence NICE. **Background:** GSTT is a teaching hospital in central London that educates gynaecologists in training as well as (GP) for specialist certification in Menopause. The menopause clinic receives approximately 580 GP referrals per month from South East London practices. The current waiting time for an initial appointment is up to 1 year. This delay reflects an increase in demand for menopause care and a deficit in service provision in many areas of the UK.NICE has recommended that GPs refer complicated cases to menopause specialists, with 11 specific criteria. **Study Sample and Data Collection:** We randomly selected 50 patients referred to the GSTT clinic by a GP between 2021 and 2022. Patient data were collected, including patient demographics, date of referral, indication for referral, date of consultation, waiting time, past medical history, investigations, and treatment instigated during the appointment. **Results:** The majority of referrals to the GSTT menopause Specialist clinic met the NICE guidelines (76%). One-sixth of the

referrals could have been prevented or managed through alternative routes. Finally, although this is a small study, some patient unmet needs (PUNS) and GPs' educational needs have been identified.

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## 16. Genetic risk impacts the association of menopausal hormone therapy with colorectal cancer risk.

**Authors:** Tian, Yu;Lin, Yi;Qu, Conghui;Arndt, Volker;Baurley, James W.;Berndt, Sonja I.;Bien, Stephanie A.;Bishop, D. Timothy;Brenner, Hermann;Buchanan, Daniel D.;Budiarto, Arif;Campbell, Peter T.;Carreras-Torres, Robert;Casey, Graham;Chan, Andrew T.;Chen, Rui;Chen, Xuechen;Conti, David V.;Diez-Obrero, Virginia;Dimou, Niki, et al

**Publication Date:** 2024

**Journal:** British Journal of Cancer

**Abstract: BACKGROUND:** Menopausal hormone therapy (MHT), a common treatment to relieve symptoms of menopause, is associated with a lower risk of colorectal cancer (CRC). To inform CRC risk prediction and MHT risk-benefit assessment, we aimed to evaluate the joint association of a polygenic risk score (PRS) for CRC and MHT on CRC risk. **METHODS:** We used data from 28,486 postmenopausal women (11,519 cases and 16,967 controls) of European descent. A PRS based on 141 CRC-associated genetic variants was modeled as a categorical variable in quartiles. Multiplicative interaction between PRS and MHT use was evaluated using logistic regression. Additive interaction was measured using the relative excess risk due to interaction (RERI). 30-year cumulative risks of CRC for 50-year-old women according to MHT use and PRS were calculated. **RESULTS:** The reduction in odds ratios by MHT use was larger in women within the highest quartile of PRS compared to that in women within the lowest quartile of PRS ( $p$ -value =  $2.7 \times 10^{-8}$ ). At the highest quartile of PRS, the 30-year CRC risk was statistically significantly lower for women taking any MHT than for women not taking any MHT, 3.7% (3.3%-4.0%) vs 6.1% (5.7%-6.5%) (difference 2.4%,  $P$ -value =  $1.83 \times 10^{-14}$ ); these differences were also statistically significant but smaller in magnitude in the lowest PRS quartile, 1.6% (1.4%-1.8%) vs 2.2% (1.9%-2.4%) (difference 0.6%,  $P$ -value =  $1.01 \times 10^{-3}$ ), indicating 4 times greater reduction in absolute risk associated with any MHT use in the highest compared to the lowest quartile of genetic CRC risk. **CONCLUSIONS:** MHT use has a greater impact on the reduction of CRC risk for women at higher genetic risk. These findings have implications for the development of risk prediction models for CRC and potentially for the consideration of genetic information in the risk-benefit assessment of MHT use. Copyright © 2024. The Author(s).

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## 17. Menopause transition and cardiovascular disease risk

**Authors:** Uddenberg, Erin R.;Safwan, Nancy;Saadedine, Mariam;Hurtado, Maria D.;Faubion, Stephanie S. and Shufelt, Chrisandra L.

**Publication Date:** Mar 22 ,2024

**Journal:** Maturitas 185, pp. 107974

**Abstract:** The risk of cardiovascular disease (CVD) notably increases in the fifth decade of a woman's life, coinciding with the onset of menopause and occurring 10 years later than the similar age-related increase in men. Menopause marks a significant transition in a woman's life and is accompanied by cardiometabolic changes, including a shift in body composition, increased blood pressure, disruptions in lipoproteins, and insulin resistance. There is increasing evidence that the menopause transition is a risk factor for CVD, independent of age-related changes, especially considering that the earlier the onset of menopause, the greater is the CVD risk. Further, menopause-related symptoms such as vasomotor symptoms, sleep disturbances, and mood changes may all have a direct impact on CVD risk. In this review, we summarize the current literature regarding CVD in midlife women, focusing on the cardiometabolic changes related to ovarian aging versus chronological aging, as well as those

related to specific menopause characteristics, including age, type of menopause and the use of menopause hormone therapy. Copyright © 2024 Elsevier B.V. All rights reserved.

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## 18. Postmenopausal endometriosis: a challenging condition beyond menopause.

**Authors:** Vallee, Alexandre;Carbonnel, Marie;Ceccaldi, Pierre-Francois;Feki, Anis and Ayoubi, Jean-Marc

**Publication Date:** 2024

**Journal:** Menopause

**Abstract: IMPORTANCE AND OBJECTIVE:** Postmenopausal endometriosis is a complex condition that challenges the conventional belief that endometriosis resolves with menopause. Despite the cessation of menstruation, a subset of women continues to experience or develop endometriosis-related symptoms during the postmenopausal period. Thus, this review aimed to shed light on postmenopausal endometriosis, exploring its clinical features, diagnostic considerations, management approaches, and the potential impact on women's health. **METHODS:** PubMed/Medline, Scopus, and Web of Science databases were used for the research, with only articles in English language, using the following terms: "postmenopausal endometriosis," "menopause," "management," "treatment," and "quality of life," from inception to 2023. **DISCUSSION AND CONCLUSION:** The clinical features of postmenopausal endometriosis include persistent or recurrent pelvic pain, dyspareunia, bowel, or urinary symptoms and, occasionally, abnormal vaginal bleeding. The absence of menstrual cycles presents a diagnostic challenge, as the traditional diagnostic criteria for endometriosis rely on menstrual patterns. Visual cues may be less evident, and the symptoms often overlap with other gynecological conditions, necessitating a thorough evaluation to differentiate postmenopausal endometriosis from other potential causes. Management approaches for postmenopausal endometriosis encompass surgical intervention, hormonal therapies, pain management, and individualized care. Postmenopausal endometriosis significantly impacts the quality of life, sexual health, and long-term well-being of women. Understanding the clinical features, diagnostic challenges, and management approaches of postmenopausal endometriosis is crucial for healthcare professionals to provide effective care and to improve the quality of life of women affected by this condition. Copyright © 2024 by The Menopause Society.

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## 19. 'But at a certain point, the lights literally went out': A qualitative study exploring midlife women's experiences of health, wellbeing, and functioning in relation to paid work.

**Authors:** Verburgh, M.;Verdonk, P.;Muntinga, M.;Van Valkengoed, I.;Hulshof, C. and Nieuwenhuijsen, K.

**Publication Date:** 2024

**Journal:** Work 77(3), pp. 799-809

**Abstract:** In the Netherlands, the fact that midlife women constitute a considerable segment of the working population is relatively new. Generally paid work contributes to midlife women's wellbeing, but they also report health challenges, such as work-related fatigue and the menopause. Objective: The objective of this study is to understand how midlife women themselves perceive their health, wellbeing, and functioning in relation to paid work.

**Methods:** In this exploratory qualitative study, 28 women participated in five ethnically homogeneous focus group discussions (FGDs). The FGDs were recorded, transcribed verbatim, and thematically analyzed using MAXQDA.

**Results:** We identified exhaustion as central to our analysis. During midlife, exhaustion seems to occur once a certain limit has been reached, both physically and mentally, with women feeling to have reached the end of their rope. Besides obvious physiological challenges, we identified two major

themes in which we discuss challenges both in paid work and private life: (1) work environment and working conditions, and (2) burdens in private life. Participants took various measures to manage and try to reduce exhaustion, including finding a new job or negotiating different job tasks, and reducing work hours.

Conclusion: This study indicates that the extent to which women experience exhaustion is associated with challenges in both paid work and private life. The underlying processes do not seem to reflect individual problems, but reflect a complex set of factors at the structural level. Nevertheless, women take several individual measures to reduce their exhaustion, including reducing their participation in paid work.

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### ***In the News:***

#### **NHS announces first ever national clinical director for women's health**

4 April 2024

"The NHS has appointed Dr Sue Mann, a consultant and lead for women's health in City and Hackney, North East London, as its first ever national clinical director for women's health

In her new role, Dr Mann will help implement the Women's Health Strategy alongside supporting the roll out of women's health hubs across England.

She will also work on the development of a network of Women's Health Champions, made up of senior leaders in every local care system to drive forward work to improve women's health."

<https://www.england.nhs.uk/2024/04/nhs-announces-first-ever-national-clinical-director-for-womens-health/>

#### **Update – Subcutaneous Hormone Implant Therapy**

2 April 2024

Julian Beach, MHRA Interim Executive Director for Healthcare Quality and Access, said: "We are committed to ensuring timely access to treatment for UK patients, and this includes HRT products." [...].

"We are aware that these unlicensed medicines are critical for a specific group of patients and as suitable alternatives are currently unavailable, further imports of these medicines to the UK market will continue while we conclude a regulatory review. We will communicate our findings once this review has concluded. In the meantime, there is no need for any action by patients."

<https://thebms.org.uk/2024/04/update-subcutaneous-hormone-implant-therapy/>

#### **NEW BMS Tool for Clinicians – HRT after myocardial infarction**

28 March 2024

"This comprehensive new BMS resource addresses key questions for healthcare professionals, including:

What does HRT do to normal arteries?

What happens when arterial disease is present?

What happens if a woman on HRT sustains an MI?

What happens if a woman with a previous MI needs HRT?

Practice points are included to guide HRT prescribing and clinical management."

<https://thebms.org.uk/wp-content/uploads/2024/03/21-BMS-TfC-HRT-after-myocardial-infarction-MARCH2024-A.pdf>

### ***Latest Menopause Exchange Newsletter***

Issue 99, Winter 2023-4

- Menopause in the workplace
- Progestogens in HRT
- Osteoporosis after the menopause
- Digestive problems at the menopause

Anyone with an interest in the menopause, midlife and post-menopausal health can receive The Menopause Exchange quarterly newsletters for FREE

[www.menopause-exchange.co.uk](http://www.menopause-exchange.co.uk) to subscribe.

### **Sources Used:**

The following were used in the creation of this bulletin: MEDLINE, Emcare, and the British Menopause Society.

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