Selección de Resúmenes de Menopausia

Semana del 11 al 17 de enero de 2023

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Does Omega-3 Fatty Acid Supplementation Have Favorable Effects on the Lipid Profile in Postmenopausal Women? A Systematic Review and Dose-Response Meta-Analysis of Randomized Controlled Trials

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Purpose: Menopause is associated with disturbances in the metabolism of lipids. Moreover, during the postmenopausal period, female subjects are more prone to develop dyslipidemia. Omega-3 fatty acids, which exert cardioprotective, anti-inflammatory, and lipid-lowering actions, are commonly recommended in postmenopausal women. However, their effect on serum lipids in this population remains unclear. This systematic review and meta-analysis of randomized controlled trials (RCTs) was conducted to clarify this research question. Methods: We systematically searched the Web of Science, Scopus, PubMed/MEDLINE, and EMBASE databases from their inception until January 3, 2022. The DerSimonian and Laird random-effects model was used to combine effect sizes. Findings: Omega-3 fatty acid supplementation resulted in a decrease in triglyceride concentrations (weighted mean difference [WMD], -17.8 mg/dL; 95% CI, -26 to -9.6; P < 0.001), particularly in the RCTs that lasted ≤16 weeks (WMD, -18.6 mg/dL), when the baseline triglyceride concentrations were ≥150 mg/dL (WMD, -22.8 mg/dL), in individuals with a body mass index ≥30 kg/m2 (WMD, -19.3 mg/dL), and when the dose of omega-3 fatty acids was ≥1 g/d (WMD, -21.10 mg/dL). LDL-C (WMD, 4.1 mg/dL; 95% CI, 1.80 to 6.36; P < 0.001) and HDL-C (WMD, 2.1 mg/dL; 95% CI, 0.97 to 3.2; P < 0.001) values increased. Total cholesterol levels (WMD, -0.15 mg/dL; 95% CI, -4 to 3.74; P = 0.94) remained unchanged after administration of omega-3 fatty acids. Implications: In postmenopausal women, supplementation with omega-3 fatty acids resulted in a significant reduction in triglyceride concentrations and a modest elevation in HDL-C and LDL-C levels, whereas this intervention did not affect total cholesterol values.

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Estrogen fluctuations during the menopausal transition are a risk factor for depressive disorders

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Women are significantly more likely to develop depression than men. Fluctuations in the ovarian estrogen hormone levels are closely linked with women's well-being. This narrative review discusses the available knowledge on the role of estrogen in modulating brain function and the correlation between changes in estrogen levels and the development of depression. Equally discussed are the possible mechanisms underlying these effects, including the role of estrogen in modulating brain-derived neurotrophic factor activity, serotonin neurotransmission, as well as the induction of inflammatory response and changes in metabolic activity, are discussed.

Hormones (Athens). 2023 Jan 13. doi: 10.1007/s42000-022-00427-1. Online ahead of print.

Hormone replacement therapy in BRCA mutation carriers: how shall we do no harm?

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Women with a BRCA mutation have an increased risk of developing breast and ovarian cancer. Bilateral salpingo-oophorectomy is the only effective strategy to reduce this risk. Risk-reducing bilateral salpingo-oophorectomy (RRSO) is recommended between the ages of 35 and 40 for women carriers of BRCA1 and between the ages of 40 and 45 for women carriers of BRCA1 and BRCA2 mutations. Most women undergo this procedure prior to their natural menopause subsequently developing an anticipated lack of hormones. This condition affects the quality of life and longevity, while it is more pronounced in women carrying a BRCA1 mutation compared to BRCA2 because they are likely to have surgery earlier. Hormone replacement therapy (HRT) is the only strategy able to significantly compensate for the loss of ovarian hormone production and counteract menopausal symptoms. There is strong evidence that short-term HRT use does not increase the risk of breast cancer among women with a BRCA1 mutation. Few data are available on BRCA2 mutation

carriers. Therefore, BRCA mutation carriers require careful counseling about the outcomes of their RRSO, including menopausal symptoms and/or the fear associated with HRT use.

Womens Health Rep (New Rochelle). 2022 Dec 15;3(1):990-997. doi: 10.1089/whr.2022.0078. eCollection 2022.

The Relationship Between Menopause and Dysphagia: A Scoping Review

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Purpose: Menopause marks the end of fertility and rapid decline of ovarian hormones in the female body, which corresponds to a myriad of changes to bodily systems, including the upper aerodigestive tract. Despite substantial evidence that menopause negatively impacts oral health, bones, and skeletal muscles, little research has examined these effects as they relate to swallowing. The purpose of this scoping review was to compile and summarize the existing literature investigating the relationship between menopause and swallowing-related structures and physiology. Methods: Search terms were selected for three databases (PubMed, Scopus, and CINAHL) to gather relevant literature evaluating the relationship between menopause and swallowing-related anatomy as well as swallowing functions in both human and animal models. Relevant articles were reviewed, collated, and summarized to synthesize findings, identify gaps in the literature, and provide suggestions for future directions. Results: This scoping review yielded 204 studies with the majority of these studies relating to one or more of the following categories: oral health, saliva, mandibular structures, and taste. Common oral symptoms reported in the literature included xerostomia, hyposalivation, tooth decay, inflammation of oral mucosa, and oral pain. Although literature supports that menopause adversely affects oral health, saliva, mandibular structures, and alters taste, a dearth of information was evident regarding how these hormone-dependent changes can adversely affect swallowing. Conclusions: The relationship between menopause and swallowing has been overlooked by field of speech-language pathology. By identifying the major gaps in the literature, these results will inform future investigations evaluating relationships among ovarian hormones and swallowing.

BMC Womens Health. 2023 Jan 13;23(1):17. doi: 10.1186/s12905-023-02162-0.

Obesity at age 20 and weight gain during adulthood increase risk of total and premature all-cause mortality: findings from women attending breast screening in Manchester

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Background: Obesity in early adulthood is associated with lower breast cancer rates in later life. This could be interpreted as a positive reinforcement of excess weight amongst younger women however, the wider implications of higher weights are less well known. This study examined the association between both obesity in early adulthood and body mass index (BMI) change through adulthood, and all-cause mortality. Methods: The Predicting Risk of Cancer At Screening (PROCAS) study recruited 57,902 women aged 46-73 years (median age 57.2, IQR 51.8-63.7 years) from the Greater Manchester National Health Service breast screening programme in North West England between 2009 and 2015. It was used to assess associations between BMI at 20 years and cohort entry with all-cause mortality ascertained via deaths recorded on the National Breast Screening System to June 2020. Hazard ratios were estimated using proportional hazards (Cox) regression adjusted for factors at entry to the cohort: age, deprivation, bilateral oophorectomy, hormone-replacement therapy, menopausal status, ethnicity, alcohol intake, physical activity, and BMI. Results: The prevalence of overweight (25-30 kg/m2) and obesity (> 30 kg/m2) were 10.4% and 2.5% respectively at 20 years, increasing to 35.2% and 25.9% respectively at cohort entry. After a mean 8.7 years follow-up we observed that overweight (HR = 1.27, 95%CI = 1.10-1.47) and obesity (HR = 2.11, 95%CI = 1.67-2.66) at 20 years had a higher mortality rate compared with healthy weight. Women who were underweight/healthy weight at 20 years and gained weight to obesity at entry had a slightly increased mortality rate compared with women who were underweight/healthy weight at both time points (HR 1.16, 95%CI = 1.02-1.32). Women with overweight (HR = 1.36, 95%CI = 1.06-1.75) or obesity (HR = 1.90, 95%CI = 1.45-2.48) at both 20 years and entry had a higher mortality rate than women who were underweight/healthy weight at both points. Conclusions: Women who self-reported overweight and obesity at 20 years had a shorter life expectancy in this cohort of women attending breast cancer screening. Weight gain from 20 years was common in this group. Girls and women should be supported to maintain a healthy weight throughout the lifespan to help increase life expectancy.

Sci Rep. 2023 Jan 11;13(1):539. doi: 10.1038/s41598-023-27731-z.

Postmenopausal hormone therapy and mortality before and after the Women's Health Initiative study

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Weighing risks and benefits of postmenopausal hormone therapy (HT) has proven a balancing act. We aimed to investigate the association between HT and mortality before and after the 2002 publication from the Women's Health Initiative (WHI) study. This publication found that the risk of using HT outweighted the benefits, and thus it caused a marked reduction in systemic HT user prevalence. The 2002 WHI publication may also have caused a change in the subsequent HT user profile, as HT is no longer recommended in the prevention of chronic diseases. This cohort study included two populations followed from 1995: A 5% random sample of female singletons from the Danish general population (n = 52,388) and a sample of Danish female twins (n = 15,261). HT use was evaluated in 1995, 2000, 2005, and 2010. The association between HT, education, and mortality was investigated and controlled for potential unobserved familial confounding in a within-pair analysis. Singletons aged 56-75 using systemic HT in 2000 had a lower mortality compared to non-users (hazard ratio (HR) 0.83, 95% confidence interval (CI) 0.78-0.89). In 2005, the mortality was like that of the background population for this age group (HR 1.02, 95% CI 0.94-1.11). Recently postmenopausal twins showed a similar tendency. Systemic HT users, who had switched to local HT by 2005, had a substantially lower mortality than non-users (HR ranging from 0.42 to 0.67 depending on age group). In conclusion, we found that the prevalence of systemic HT use declined after 2002, and systemic HT users' mortality changed from lower before 2002 to similar to that of the background population after 2002. This indicates that the healthiest users decided to either drop systemic HT or switcted to local HT, as recommendations changed following the WHI publication.

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Use of exogenous hormones in those at increased risk for breast cancer: contraceptive and menopausal hormones in gene carriers and other high-risk patients

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Importance and objective: Addressing the hormonal needs of individuals at increased risk of breast cancer (BC) can be a challenge. Observational, prospective, and case-control data support the safety of hormonal contraception in women, often with the added benefits of ovarian and endometrial cancer risk reduction. The majority of data on menopausal hormone therapy (HT) in the highest-risk patients comes from studies of patients with pathogenic variants in BRCA1 and BRCA2 who undergo early surgical menopause. The benefits of risk-reducing salpingo-oophorectomy are not minimized by HT, whereas its use mitigates accelerated osteoporosis and cardiovascular disease. In other patients at increased risk, such as with family history, studies have shown little risk with significant benefit. Methods: We review evidence to help women's health practitioners aid patients in making choices. The paper is divided into four parts: 1, contraception in the very high-risk patient (ie, with a highly penetrant BC predisposition gene); 2, contraception in other patients at increased risk; 3, menopausal HT in the gene carrier; and 4, HT in other high-risk patients. Discussion and conclusion: Women at increased risk for BC both early and later in life should be offered reassurance around the use of premenopausal and postmenopausal hormone therapies. The absolute risks associated with these therapies are low, even in the very high-risk patient, and the benefits are often substantial. Shared decision making is key in presenting options, and knowledge of the data in this area is fundamental to these discussions.

Alzheimers Res Ther. 2023 Jan 9;15(1):10. doi: 10.1186/s13195-022-01121-5.

Hormone replacement therapy is associated with improved cognition and larger brain volumes in at-risk APOE4 women: results from the European Prevention of Alzheimer's Disease (EPAD) cohort

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Background: The risk of dementia is higher in women than men. The metabolic consequences of estrogen decline during menopause accelerate neuropathology in women. The use of hormone replacement therapy (HRT) in the prevention of cognitive decline has shown conflicting results. Here we investigate the modulating role of APOE genotype and age at HRT initiation on the heterogeneity in cognitive response to HRT. Methods: The analysis used baseline data from participants in the European Prevention of Alzheimer's Dementia (EPAD) cohort (total n= 1906, women= 1178, 61.8%). Analysis of covariate (ANCOVA) models were employed to test the independent and interactive impact of APOE genotype and HRT on select cognitive tests, such as MMSE, RBANS, dot counting, Four Mountain Test (FMT), and the supermarket trolley test (SMT), together with volumes of the medial temporal lobe (MTL) regions by MRI. Multiple linear regression models were used to examine the impact of age of HRT initiation according to APOE4 carrier status on these cognitive and MRI outcomes. Results: APOE4 HRT users had the highest RBANS delayed memory index score (P-APOE*HRT

interaction = 0.009) compared to APOE4 non-users and to non-APOE4 carriers, with 6-10% larger entorhinal (left) and amygdala (right and left) volumes (P-interaction= 0.002, 0.003, and 0.005 respectively). Earlier introduction of HRT was associated with larger right (standardized β= -0.555, p=0.035) and left hippocampal volumes (standardized β= -0.577, p=0.028) only in APOE4 carriers. Conclusion: HRT introduction is associated with improved delayed memory and larger entorhinal and amygdala volumes in APOE4 carriers only. This may represent an effective targeted strategy to mitigate the higher life-time risk of AD in this large at-risk population subgroup. Confirmation of findings in a fit for purpose RCT with prospective recruitment based on APOE genotype is needed to establish causality.

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Age at Natural Menopause Impacts Cerebrovascular Reactivity and Brain Structure

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Menopause is associated with adverse changes in vascular health coinciding with an increased risk of stroke and vascular cognitive impairment. However, there is significant variation in the age at menopause. The present study examined how the age at natural menopause impacts cerebrovascular reactivity and structural biomarkers of brain aging. Thirty-five healthy postmenopausal women were classified as early onset menopause (Early; n = 19, age at menopause: 47 ± 2 years) or later onset menopause (Late; n = 16, age at menopause: 55 ± 2 years). Middle cerebral artery blood velocity (MCAv), mean arterial blood pressure (MAP), and end-tidal carbon dioxide ($ETCO_2$) were recorded during a stepped hypercapnia protocol. Reactivity was calculated as the slope of the relationship between $ETCO_2$ and each variable of interest. Brain volumes and white matter hyperintensities (WMH) were obtained with 3T MRI. Resting MAP was greater in the Early group (99 ± 9 mmHg) compared with the Late group (90 ± 12 mmHg; P = 0.02). Cerebrovascular reactivity, assessed using MCAv, was blunted in the Early group (1.87 ± 0.92 cm/s/mmHg) compared to the Late group (2.37 ± 0.75 cm/s/mmHg; P = 0.02). Total brain volume did not differ between groups (Early: 1.08 ± 0.07L vs. Late: 1.07 ± 0.06L; P = 0.66), but the Early group demonstrated greater WMH fraction compared with the Late group (Early: 0.36 ± 0.14% vs. Late: 0.25 ± 0.14%; P = 0.02). These results suggest that age at natural menopause impacts cerebrovascular function and WMH burden in healthy postmenopausal.

Maturitas. 2022 Dec 23;169:10-15. doi: 10.1016/j.maturitas.2022.12.001. Online ahead of print.

The association between postpartum depression and perimenopausal depression: A nationwide register-based cohort study

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Objectives: The purpose of the study was to investigate whether postpartum depression is associated with a risk of depression during perimenopause.Study design: This is a Danish nationwide register-based cohort study of 270,613 individuals who were born in 1 960-1968, who gave birth to a liveborn child recorded in the Medical Birth Register before the age of 40, and who lived in Denmark when turning 47 years old. The association between postpartum depression and depression during perimenopause was analyzed using a Cox Proportional Hazards model adjusted for education level, marital status, and age at first delivery.Main outcome measures: Depression during perimenopause was identified by a diagnosis of depression during nine years of follow-up registered in the Danish National Patient Registry. Results: A total of 7694 (2.9 %) study participants were diagnosed with depression during perimenopause. Postpartum depression was associated with 12.82 [95 % confidence interval (CI): 8.93;18.41] times higher hazard of depression during perimenopause, while depression prior to study baseline was associated with 11.91 [95 % CI: 11.14;12.73] times higher hazard compared with individuals with no history of depression. There was no difference in the association between postpartum depression and depression prior to study baseline for depression during perimenopause. Conclusion: Prior depression, no matter the timing, is associated with markedly higher risk of depression during perimenopause. Thus, individuals who have experienced postpartum depression do not experience a greater risk of depression during perimenopause compared with individuals who have experienced depression unrelated to periods of hormonal changes during their fertile life.