The effect of calcium supplementation in people under 35 years old: A systematic review and meta-analysis of randomized controlled trials

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Background: The effect of calcium supplementation on bone mineral accretion in people under 35 years old is inconclusive. To comprehensively summarize the evidence for the effect of calcium supplementation on bone mineral accretion in young populations (≤35 years). Methods: This is a systematic review and meta-analysis. The Pubmed, Embase, ProQuest, CENTRAL, WHO Global Index Medicus, Clinical Trials.gov, WHO ICTRP, China National Knowledge Infrastructure (CNKI), and Wanfang Data databases were systematically searched from database inception to April 25, 2021. Randomized clinical trials assessing the effects of calcium supplementation on bone mineral density (BMD) or bone mineral content (BMC) in people under 35 years old. Results: This systematic review and meta-analysis identified 43 studies involving 7,382 subjects. Moderate certainty of evidence showed that calcium supplementation was associated with the accretion of BMD and BMC, especially on femoral neck (standardized mean difference [SMD] 0.627, 95% confidence interval [CI] 0.338-0.915; SMD 0.364, 95% CI 0.134-0.595; respectively) and total body (SMD 0.330, 95% CI 0.163-0.496; SMD 0.149, 95% CI 0.006-0.291), also with a slight improvement effect on lumbar spine BMC (SMD 0.163, 95% CI 0.008-0.317), no effects on total hip BMD and BMC and lumbar spine BMD were observed. Very interestingly, subgroup analyses suggested that the improvement of bone at femoral neck was more pronounced in the peripeak bone mass (PBM) population (20-35 years) than the pre-PBM population (<20 years). Conclusions: Our findings provided novel insights and evidence in calcium supplementation, which shown that calcium supplementation significantly improves bone mass, implying that preventive calcium supplementation before or around achieving PBM may be a shift in the window of intervention for osteoporosis.

The Portfolio Diet and Incident Type 2 Diabetes: Findings from the Women's Health Initiative Prospective Cohort Study

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Objective: A plant-based dietary pattern, the Portfolio Diet, has been shown to lower LDL cholesterol and other cardiovascular disease risk factors. However, no study has evaluated the association of this diet with incident type 2 diabetes. Research design and methods: This analysis included 145,299 postmenopausal women free of diabetes at baseline in the Women's Health Initiative (WHI) Clinical Trials and Observational Study from 1993 to 2021. Adherence to the diet was assessed with a score based on six components (high in plant protein [soy and pulses], nuts, viscous fiber, plant sterols, and monounsaturated fat and low in saturated fat and cholesterol) determined from a validated food-frequency questionnaire. We used Cox proportional hazards models to estimate hazard ratios (HRs) and 95% CIs of the association of the Portfolio Diet, alongside the Dietary Approaches to Stop Hypertension (DASH) and Mediterranean diets, with incident type 2 diabetes, with adjustment for potential confounders. Results: Over a mean follow-up of 16.0 years, 13,943 cases of incident type 2 diabetes were identified. In comparisons of the highest with the lowest quintiles of adherence, the HRs for risk of incident type 2 diabetes were 0.77 (95% CI 0.72, 0.82) for the Portfolio Diet, 0.69 (0.64, 0.73) for the DASH diet, and 0.78 (0.74, 0.83) for the Mediterranean diet. These findings were attenuated by 10% after additional adjustment for BMI. Conclusions: Greater adherence to the plant-predominant Portfolio, DASH, and Mediterranean diets was prospectively associated with lower risk of type 2 diabetes in postmenopausal women.
Age at Menarche and Menopause, Reproductive Lifespan, and Risk of Cardiovascular Events Among Chinese Postmenopausal Women: Results From a Large National Representative Cohort Study

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Background: At present, the association between age at menarche and menopause, reproductive lifespan, and cardiovascular disease (CVD) risk among Chinese postmenopausal women is not clear, and some related researches are contradictory. Methods: A total of 6,198 Chinese postmenopausal women with a mean age of 63.6 years were enrolled at baseline in 2012-2015 and followed up for 5 years. A standardized questionnaire was used to collect relevant information by well-trained interviewers. Physical examination of the participants was performed by trained medical staff. CVD events were observed during follow-up. Cox proportional hazards models were used to estimate hazard ratios between reproductive characteristics and CVD events. Results: Age at menarche was positively associated with CVD events (HR, 1.106; 95% CI, 1.047-1.167). There was a negative association between age at menopause and CVD risk in postmenopausal women with comorbidity (HR, 0.952; 95% CI, 0.909-0.996). Reproductive lifespan was negatively associated with CVD events (HR, 0.938; 95% CI, 0.880-0.999). The CVD risk increased by 10.6% for every 1-year increase in age at menarche. The CVD risk reduced by 6.2% for every 1-year increase in age at menopause in women with comorbidity. The CVD risk reduced by 3.8% for every 1-year increase in reproductive lifespan. Conclusions: Based on the large prospective study with a nationally representative sample, Chinese postmenopausal women with late age at menarche and shorter reproductive lifespan have higher risk of CVD events.


Self-reported menstrual cycle length during reproductive years in relation to menopausal symptoms at midlife in Project Viva

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Objective: The aim of this study was to investigate the extent to which self-reported menstrual cycle length during reproductive years is associated with menopausal symptoms and age at natural menopause at midlife. Methods: This analysis includes 634 women who enrolled in Project Viva during pregnancy (1999-2002) and completed the midlife visit approximately 18 years later. Women self-reported menstrual cycle length at enrollment (early pregnancy) and at midlife reported total and specific menopausal symptoms using the Menopause Rating Scale as well as age at natural menopause. We used linear and regression models to evaluate associations of cycle length with total and specific menopausal symptoms. We also applied a time-to-event Cox proportional hazards model to investigate the relationship between menstrual cycle length and onset of natural menopause. We adjusted models for age at midlife visit, prepregnancy body mass index, race/ethnicity, education, and parity. Results: At enrollment (median age, 33.3 years), 90 (14%) women reported having short (≤25 days) and 39 (6%) reported long (≥35 days) menstrual cycles. Compared with women with a normal menstrual cycle length of 26 to 34 days, women whose cycles were short had a higher total Menopause Rating Scale at midlife (β = 2.05; 95% confidence interval [CI], 0.73-3.38). Specifically, women with short menstrual cycles during their reproductive years had higher odds of midlife sleep problems (odds ratio [OR], 1.92; 95% CI, 1.10-3.37), heart discomfort (OR, 1.68; 95% CI, 1.03-2.73), and depressive symptoms (OR, 1.85; 95% CI, 1.16-2.96). In addition, compared with women with a normal cycle length of 26 to 34 days, women reporting short cycles had an earlier onset of natural menopause (hazard ratio, 1.67; 95% CI, 1.11-2.51). Conclusions: Compared with women with normal menstrual cycle length, those with short menstrual cycles during their reproductive years had a higher frequency of total and certain menopausal symptoms at midlife and reached menopause earlier.


Perception of higher frequency of daily hot flashes in 50-year-old women today: a study of trends over time during 48 years in the Population Study of Women in Gothenburg, Sweden

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Objective: The aim of this study was to examine if there are any differences in the prevalence of daily hot flashes in 50-year-old women in a longitudinal perspective (from 1968 to 2017). Methods: Cohort comparisons of four population-based samples of 50-year-old women born in 1918, 1930 (earlier-born cohorts), 1954, and 1966 (later-born cohorts) from the Prospective Population Study of Women in Gothenburg examined in 1968-1969, 1980-1981, 2004-
2005, and 2016-2017. Questions about frequency of hot flashes have been formulated in the same way throughout all follow-up examinations. Changes between four generations of 50-year-old women were studied. Results: In the unadjusted model, we found an increased prevalence of daily hot flashes in 50-year-old women born in 1954 and 1966 compared with 50-year-old women born in 1918 and 1930 (odds ratio, 1.74; 95% confidence interval, 1.37-2.22). When considering potential predictors for daily hot flashes (smoking, perceived level of high stress, BMI, waist-to-hip ratio, hormone therapy, and hormonal contraceptives) in the adjusted model, there was a notable difference; odds ratio increases from 1.74 to 1.92 (95% confidence interval, 1.46-2.52). Smoking frequency was substantially lower in the later-born cohorts, 39% compared with 17%. Conclusions: In this prospective longitudinal study of 50-year-old women, we found nearly twice as high odds of reporting daily hot flashes in the later-born women compared with earlier-born. When controlling for potential predictors, there was still an obvious difference, which cannot be explained in our study. These findings have not earlier been described, and there is a need for further longitudinal population studies investigating the prevalence of hot flashes over time. Moreover, additional research is required exploring the underlying mechanism of hot flashes, as well as studies that take into account potential risk factors in the environment and societal development over time, that is, impacts of endocrine-disrupting chemicals changes in lifestyle, environmental, and dietary factors, as well as working conditions.


Comparison of Severity of Genitourinary Syndrome of Menopause Symptoms After Carbon Dioxide Laser vs Vaginal Estrogen Therapy: A Systematic Review and Meta-analysis

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Importance: Vaginal estrogen for genitourinary syndrome of menopause (GSM) should be used with caution in women with contraindications, highlighting the need for effective treatment alternatives. Objective: To compare the severity of GSM after vaginal laser vs estrogen therapy. Data sources: The PubMed, Embase, and Cochrane Library databases were searched for articles published from database inception to April 8, 2022, with no language restrictions. Reference lists were also searched. Study selection: Randomized clinical trials (RCTs) that compared the use of lasers with vaginal estrogen in adults were selected. Data extraction and synthesis: Two investigators independently extracted data from included studies. The Cochrane risk of bias tool for RCTs was used to assess risk of bias of each study. A random-effects model was used to pool mean differences (MDs) with 95% CIs. Main outcomes and measures: Primary outcomes were Vaginal Analog Scale (VAS; higher scores indicate severer symptoms), Vaginal Health Index (VHI; higher scores indicate better vaginal health), Vaginal Maturation Index (VMI; higher scores indicate higher estrogen effect on the vaginal epithelium), Female Sexual Function Index (FSFI; higher scores indicate better female sexual function), and Sexual Quotient-Female (SQ-F; higher scores indicate better female sexual function) questionnaire scores. Urinary symptoms were assessed as an additional outcome. Data analyses were performed from April 9 to 12, 2022. Results: A total of 6 RCTs with 270 women with GSM were included (135 were randomized to laser therapy and 135 to estrogen therapy; mean age ranged from 54.6 to 61.0 years). No significant differences were found between carbon dioxide laser and vaginal estrogen from baseline to the end of follow-up in overall VAS scores (MD, -0.16; 95% CI, -0.67 to 0.36; I², 33.31%), VHI (MD, 0.20; 95% CI, -0.56 to 0.97; I², 83.25%), VMI (MD, -0.56; 95% CI, -1.14 to 0.02; I², 35.07%), FSFI (MD, -0.04; 95% CI, -0.45 to 0.36; I², 41.60%), and SQ-F (P = .37 based on 1 study). Other questionnaire-based outcome measures demonstrated no difference between groups from baseline to the end of follow-up for changes in urinary symptoms. Conclusions and relevance: This systematic review and meta-analysis of RCTs found that vaginal laser treatment is associated with similar improvement in genitourinary symptoms as vaginal estrogen therapy. Further research is needed to test whether vaginal laser therapy could be a potential treatment option for women with contraindications to vaginal estrogen.