 **Selección de Resúmenes de Menopausia**

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[**Eur J Med Chem.**](http://www.ncbi.nlm.nih.gov/pubmed/24974351)**2014 Jun 17;83C:317-337. doi: 10.1016/j.ejmech.2014.06.036. [Epub ahead of print]**

**Novel, potent and selective 17β-hydroxysteroid dehydrogenase type 2 inhibitors as potential therapeutics for osteoporosis with dual human and mouse activities.**

[Perspicace E](http://www.ncbi.nlm.nih.gov/pubmed?term=Perspicace%20E%5BAuthor%5D&cauthor=true&cauthor_uid=24974351)1, [Cozzoli L](http://www.ncbi.nlm.nih.gov/pubmed?term=Cozzoli%20L%5BAuthor%5D&cauthor=true&cauthor_uid=24974351)2, [Gargano EM](http://www.ncbi.nlm.nih.gov/pubmed?term=Gargano%20EM%5BAuthor%5D&cauthor=true&cauthor_uid=24974351)1, [Hanke N](http://www.ncbi.nlm.nih.gov/pubmed?term=Hanke%20N%5BAuthor%5D&cauthor=true&cauthor_uid=24974351)3, [Carotti A](http://www.ncbi.nlm.nih.gov/pubmed?term=Carotti%20A%5BAuthor%5D&cauthor=true&cauthor_uid=24974351)4, [Hartmann RW](http://www.ncbi.nlm.nih.gov/pubmed?term=Hartmann%20RW%5BAuthor%5D&cauthor=true&cauthor_uid=24974351)5, [Marchais-Oberwinkler S](http://www.ncbi.nlm.nih.gov/pubmed?term=Marchais-Oberwinkler%20S%5BAuthor%5D&cauthor=true&cauthor_uid=24974351)6.

17β-Hydroxysteroid dehydrogenase type 2 (17β-HSD2) is responsible for the oxidation of the highly active estradiol (E2) and testosterone (T) into the less potent estrone (E1) and Δ4-androstene-3,17-dione (Δ4-AD), respectively. As 17β-HSD2 is present in bones and as estradiol and testosterone are able to induce bone formation and repress bone resorption, inhibition of this enzyme could be a new promising approach for the treatment of osteoporosis. Herein, we describe the design, the synthesis and the biological evaluation of 24 new 17β-HSD2 inhibitors in the 5-substituted thiophene-2-carboxamide class. Structure-activity and structure-selectivity relationships have been explored by variation of the sulfur atom position in the central core, exchange of the thiophene by a thiazole, substitution of the amide group with a larger moiety, exchange of the N-methylamide group with bioisosteres like N-methylsulfonamide, N-methylthioamide and ketone, and substitutions at positions 2 and 3 of the thiophene core with alkyl and phenyl groups leading to 2,3,5-trisubstituted thiophene derivatives. The compounds were evaluated on human and mouse enzymes. From this study, a novel highly potent and selective compound in both human and mouse 17β-HSD2 enzymes was identified, compound 21 (IC50(h17β-HSD2) = 235 nM, selectivity factor toward h17β-HSD1 = 95, IC50 (m17β-HSD2) = 54 nM). This new compound 21 could be used for an in vivo proof of principle to demonstrate the true therapeutic efficacy of 17β-HSD2 inhibitors in osteoporosis. New structural insights into the active sites of the human and mouse enzymes were gained.

[**Lancet Diabetes Endocrinol.**](http://www.ncbi.nlm.nih.gov/pubmed/24974252)**2014 Jun 25. pii: S2213-8587(14)70113-5. [Epub ahead of print]**

**Association of vitamin D status with arterial blood pressure and hypertension risk: a mendelian randomisation study.**

[Vimaleswaran KS](http://www.ncbi.nlm.nih.gov/pubmed?term=Vimaleswaran%20KS%5BAuthor%5D&cauthor=true&cauthor_uid=24974252)1, [Cavadino A](http://www.ncbi.nlm.nih.gov/pubmed?term=Cavadino%20A%5BAuthor%5D&cauthor=true&cauthor_uid=24974252)2, [Berry DJ](http://www.ncbi.nlm.nih.gov/pubmed?term=Berry%20DJ%5BAuthor%5D&cauthor=true&cauthor_uid=24974252)2; [LifeLines, et al. Cohort Study investigators](http://www.ncbi.nlm.nih.gov/pubmed?term=LifeLines%20Cohort%20Study%20investigators%5BCorporate%20Author%5D).

BACKGROUND: Low plasma 25-hydroxyvitamin D (25[OH]D) concentration is associated with high arterial blood pressure and hypertension risk, but whether this association is causal is unknown. We used a mendelian randomisation approach to test whether 25(OH)D concentration is causally associated with blood pressure and hypertension risk. METHODS: In this mendelian randomisation study, we generated an allele score (25[OH]D synthesis score) based on variants of genes that affect 25(OH)D synthesis or substrate availability (CYP2R1 and DHCR7), which we used as a proxy for 25(OH)D concentration. We meta-analysed data for up to 108 173 individuals from 35 studies in the D-CarDia collaboration to investigate associations between the allele score and blood pressure measurements. We complemented these analyses with previously published summary statistics from the International Consortium on Blood Pressure (ICBP), the Cohorts for Heart and Aging Research in Genomic Epidemiology (CHARGE) consortium, and the Global Blood Pressure Genetics (Global BPGen) consortium. FINDINGS: In phenotypic analyses (up to n=49 363), increased 25(OH)D concentration was associated with decreased systolic blood pressure (β per 10% increase, -0·12 mm Hg, 95% CI -0·20 to -0·04; p=0·003) and reduced odds of hypertension (odds ratio [OR] 0·98, 95% CI 0·97-0·99; p=0·0003), but not with decreased diastolic blood pressure (β per 10% increase, -0·02 mm Hg, -0·08 to 0·03; p=0·37). In meta-analyses in which we combined data from D-CarDia and the ICBP (n=146 581, after exclusion of overlapping studies), each 25(OH)D-increasing allele of the synthesis score was associated with a change of -0·10 mm Hg in systolic blood pressure (-0·21 to -0·0001; p=0·0498) and a change of -0·08 mm Hg in diastolic blood pressure (-0·15 to -0·02; p=0·01). When D-CarDia and consortia data for hypertension were meta-analysed together (n=142 255), the synthesis score was associated with a reduced odds of hypertension (OR per allele, 0·98, 0·96-0·99; p=0·001). In instrumental variable analysis, each 10% increase in genetically instrumented 25(OH)D concentration was associated with a change of -0·29 mm Hg in diastolic blood pressure (-0·52 to -0·07; p=0·01), a change of -0·37 mm Hg in systolic blood pressure (-0·73 to 0·003; p=0·052), and an 8·1% decreased odds of hypertension (OR 0·92, 0·87-0·97; p=0·002). INTERPRETATION: Increased plasma concentrations of 25(OH)D might reduce the risk of hypertension. This finding warrants further investigation in an independent, similarly powered study.

[**BMC Public Health.**](http://www.ncbi.nlm.nih.gov/pubmed/24969543)**2014 Jun 26;14:554. doi: 10.1186/1471-2458-14-554.**

**Consumption of sweet foods and mammographic breast density: a cross-sectional study.**

[Duchaine CS](http://www.ncbi.nlm.nih.gov/pubmed?term=Duchaine%20CS%5BAuthor%5D&cauthor=true&cauthor_uid=24969543), [Dumas I](http://www.ncbi.nlm.nih.gov/pubmed?term=Dumas%20I%5BAuthor%5D&cauthor=true&cauthor_uid=24969543), [Diorio C](http://www.ncbi.nlm.nih.gov/pubmed?term=Diorio%20C%5BAuthor%5D&cauthor=true&cauthor_uid=24969543)1.

BACKGROUND: The increasing consumption of sugar worldwide seems to lead to several health problems, including some types of cancer. While some studies reported a positive association between sweet foods intake and breast cancer risk, little is known about their relation to mammographic density (MD), a strong breast cancer risk factor. This study examined the association of sweet foods and drinks intake with MD among 776 premenopausal and 779postmenopausal women recruited at mammography. METHODS: A food-frequency questionnaire was used to assess intake of sweet foods, sugar-sweetened beverages and spoonsful of sugar added. Percent and absolute breast density were estimated using a computer-assisted method. Multivariate generalized linear models were used to evaluate associations. All models were adjusted for potential confounders, including age and body mass index. RESULTS: For increasing quartiles of sugar-sweetened beverages intake, adjusted-mean absolute density was respectively 32, 34, 32 and 36 cm2 among all women (Ptrend = 0.040) and 43, 46, 44 and 51 cm2 among premenopausal women (Ptrend = 0.007). For increasing quartiles of sweet foods intake, adjusted-mean percent density was respectively 16, 16, 17 and 19% amongpostmenopausal women (Ptrend = 0.036). No association was shown between intake of spoonsful of sugar added and MD. CONCLUSION: Our results suggest that an increase in sweet foods or sugar-sweetened beverage intake is associated with higher MD.

[**Climacteric.**](http://www.ncbi.nlm.nih.gov/pubmed/24969415)**2014 Jun 27:1-17. [Epub ahead of print]**

**Prevention of diseases after menopause.**

[Lobo RA](http://www.ncbi.nlm.nih.gov/pubmed?term=Lobo%20RA%5BAuthor%5D&cauthor=true&cauthor_uid=24969415)1, [Davis SR](http://www.ncbi.nlm.nih.gov/pubmed?term=Davis%20SR%5BAuthor%5D&cauthor=true&cauthor_uid=24969415), [De Villiers TJ](http://www.ncbi.nlm.nih.gov/pubmed?term=De%20Villiers%20TJ%5BAuthor%5D&cauthor=true&cauthor_uid=24969415), [Gompel A](http://www.ncbi.nlm.nih.gov/pubmed?term=Gompel%20A%5BAuthor%5D&cauthor=true&cauthor_uid=24969415), [Henderson VW](http://www.ncbi.nlm.nih.gov/pubmed?term=Henderson%20VW%5BAuthor%5D&cauthor=true&cauthor_uid=24969415), [Hodis HN](http://www.ncbi.nlm.nih.gov/pubmed?term=Hodis%20HN%5BAuthor%5D&cauthor=true&cauthor_uid=24969415), [Lumsden MA](http://www.ncbi.nlm.nih.gov/pubmed?term=Lumsden%20MA%5BAuthor%5D&cauthor=true&cauthor_uid=24969415), [Mack WJ](http://www.ncbi.nlm.nih.gov/pubmed?term=Mack%20WJ%5BAuthor%5D&cauthor=true&cauthor_uid=24969415),et al.

Women may expect to spend more than a third of their lives after menopause. Beginning in the sixth decade, many chronic diseases will begin to emerge, which will affect both the quality and quantity of a woman's life. Thus, the onset of menopause heralds an opportunity for prevention strategies to improve the quality of life and enhance longevity. Obesity, metabolic syndrome and diabetes, cardiovascular disease, osteoporosis and osteoarthritis, cognitive decline, dementia and depression, and cancer are the major diseases of concern. Prevention strategies at menopausehave to begin with screening and careful assessment for risk factors, which should also include molecular and genetic diagnostics, as these become available. Identification of certain risks will then allow directed therapy. Evidence-based prevention for the diseases noted above include lifestyle management, cessation of smoking, curtailing excessive alcohol consumption, a healthy diet and moderate exercise, as well as mentally stimulating activities. Although the most recent publications from the follow-up studies of the Women's Health Initiative do not recommendmenopause hormonal therapy as a prevention strategy, these conclusions may not be fully valid for midlife women, on the basis of the existing data. For healthy women aged 50-59 years, estrogen therapy decreases coronary heart disease and all-cause mortality; this interpretation is entirely consistent with results from other randomized, controlled trials and observational studies. Thus. as part of a comprehensive strategy to prevent chronic disease after menopause, menopausal hormone therapy, particularly estrogen therapy may be considered as part of the armamentarium.

[**Value Health.**](http://www.ncbi.nlm.nih.gov/pubmed/24969003)**2014 Jun;17(4):424-32. doi: 10.1016/j.jval.2014.01.008. Epub 2014 May 5.**

**Bazedoxifene versus Oral Bisphosphonates for the Prevention of Nonvertebral Fractures in Postmenopausal Women with Osteoporosis at Higher Risk of Fracture: A Network Meta-Analysis.**

[Ellis AG](http://www.ncbi.nlm.nih.gov/pubmed?term=Ellis%20AG%5BAuthor%5D&cauthor=true&cauthor_uid=24969003)1, [Reginster JY](http://www.ncbi.nlm.nih.gov/pubmed?term=Reginster%20JY%5BAuthor%5D&cauthor=true&cauthor_uid=24969003)2, [Luo X](http://www.ncbi.nlm.nih.gov/pubmed?term=Luo%20X%5BAuthor%5D&cauthor=true&cauthor_uid=24969003)3, [Cappelleri JC](http://www.ncbi.nlm.nih.gov/pubmed?term=Cappelleri%20JC%5BAuthor%5D&cauthor=true&cauthor_uid=24969003)3, [Chines A](http://www.ncbi.nlm.nih.gov/pubmed?term=Chines%20A%5BAuthor%5D&cauthor=true&cauthor_uid=24969003)4, [Sutradhar S](http://www.ncbi.nlm.nih.gov/pubmed?term=Sutradhar%20S%5BAuthor%5D&cauthor=true&cauthor_uid=24969003)5, [Jansen JP](http://www.ncbi.nlm.nih.gov/pubmed?term=Jansen%20JP%5BAuthor%5D&cauthor=true&cauthor_uid=24969003)6.

OBJECTIVE: To compare the efficacy of bazedoxifene and oral bisphosphonates for the prevention of nonvertebral fractures (NVFs) in women with higher risk of postmenopausal osteoporosis (i.e., the Fracture Risk Assessment Tool [FRAX] score ≥ 20%), based on currently available evidence from randomized controlled trials. METHODS: Randomized controlled trials evaluating the NVF relative risk reduction (RRR) with oral bisphosphonates or bazedoxifene were identified by a systematic literature review and combined by means of a network meta-analysis. A subgroup of patients with a FRAX score of 20% or more in the bazedoxifene phase III osteoporosis study was selected as the population of interest on the basis of the bazedoxifene label. In one analysis (analysis 1), the placebo response of the subgroup with a FRAX score of 20% or more was the benchmark to select comparable bisphosphonate trials. Additional analyses incorporated the aggregate data from the bisphosphonate trials with all the FRAX subgroups (analysis 2) or with the individual patient data from the bazedoxifene trial (analysis 3). RESULTS: Nine identified bisphosphonate trials (alendronate, ibandronate, risedronate; N = 23,440 patients) with a similar placebo response as observed for the subgroup of high risk patients in the bazedoxifene trial were included in analysis 1. The results of the network meta-analysis of this study set suggest that bazedoxifene is expected to have an RRR of 0.43 (95% credible interval [CrI] -0.19 to 0.72) versus alendronate, 0.58 (95% CrI 0.05-0.81) versus ibandronate, and 0.39 (95% CrI -0.29 to 0.70) versus risedronate. Analyses in which treatment effects with bisphosphonates were projected to a population with a FRAX score of 20% or more with meta-regression approaches (analysis 2 and analysis 3) provide similar findings. CONCLUSION: Based on an indirect comparison of randomized trials, bazedoxifene is expected to have at least a comparable RRR of NVF as alendronate, ibandronate, and risedronate in women with higher risk of postmenopausal osteoporosis.

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**Distinct role of estrogen receptor-alpha and beta on postmenopausaldiabetes-induced vascular dysfunction.**

[Bansal S](http://www.ncbi.nlm.nih.gov/pubmed?term=Bansal%20S%5BAuthor%5D&cauthor=true&cauthor_uid=24967951)1, [Chopra K](http://www.ncbi.nlm.nih.gov/pubmed?term=Chopra%20K%5BAuthor%5D&cauthor=true&cauthor_uid=24967951)2.

Estrogen is known to influence vascular functions and insulin sensitivity, but the relative contribution of estrogen receptor (ER) isoforms in postmenopausal diabetes-induced vascular dysfunction is unclear. The aim of the present study was to delineate the distinct role of estrogen receptor-α and beta β on the vascular function in ovariectomized diabetic rats. Age matched 60 female sprague dawley rats (200-250g) were divided in nine groups. Bilateral ovariectomy was performed and streptozotocin was used to induce experimental diabetes. Rats were administered with 10μg/kg/s.c. of a nonselective estrogen receptor agonist, 17-β estradiol (E2), selective ER-α agonist (4,4',4″-(4-propyl-[1H] pyrazole-1,3,5-triyl) tris phenol (PPT) and selective ER-β agonist, 2,3-bis(4-hydroxyphenyl)-propionitrile (DPN) for 4weeks after STZ injection. Treatment with selective ER-α agonist and E2 improved the impaired glycemic and lipid profile in ovariectomized diabetic rats, however selective ER-β agonist did not show any effect. Vascular endothelial dysfunction was assessed by acetylcholine and sodium nitroprusside-induced endothelium dependent and independent relaxation in isolated rat aortic ring preparation as well as by electron microscopy of thoracic aorta. Further, serum thiobarbituric acid reactive substances, tumour necrotic factor-alpha and interleukin-1 beta and C-reactive protein were estimated to assess oxidative stress and vascular inflammation. Treatment with ER-α agonist markedly and E2 partially improved vascular function and endothelial integrity along with reduction in serum TBARS and inflammatory cytokines. However, ER-β agonist did not show any improvement in vascular functions, oxidative stress or inflammation. These findings suggest that selective targeting of ER-α receptors results in vasculoprotection in the state of hypoestrogenicity and diabetes.

[**Int Urogynecol J.**](http://www.ncbi.nlm.nih.gov/pubmed/24964761)**2014 Jun 26. [Epub ahead of print]**

**Hysterectomy and urinary incontinence in postmenopausal women.**

[Kudish BI](http://www.ncbi.nlm.nih.gov/pubmed?term=Kudish%20BI%5BAuthor%5D&cauthor=true&cauthor_uid=24964761)1, [Shveiky D](http://www.ncbi.nlm.nih.gov/pubmed?term=Shveiky%20D%5BAuthor%5D&cauthor=true&cauthor_uid=24964761), [Gutman RE](http://www.ncbi.nlm.nih.gov/pubmed?term=Gutman%20RE%5BAuthor%5D&cauthor=true&cauthor_uid=24964761), [Jacoby V](http://www.ncbi.nlm.nih.gov/pubmed?term=Jacoby%20V%5BAuthor%5D&cauthor=true&cauthor_uid=24964761), [Sokol AI](http://www.ncbi.nlm.nih.gov/pubmed?term=Sokol%20AI%5BAuthor%5D&cauthor=true&cauthor_uid=24964761), [Rodabough R](http://www.ncbi.nlm.nih.gov/pubmed?term=Rodabough%20R%5BAuthor%5D&cauthor=true&cauthor_uid=24964761), [Howard BV](http://www.ncbi.nlm.nih.gov/pubmed?term=Howard%20BV%5BAuthor%5D&cauthor=true&cauthor_uid=24964761), [Blanchette P](http://www.ncbi.nlm.nih.gov/pubmed?term=Blanchette%20P%5BAuthor%5D&cauthor=true&cauthor_uid=24964761), [Iglesia CB](http://www.ncbi.nlm.nih.gov/pubmed?term=Iglesia%20CB%5BAuthor%5D&cauthor=true&cauthor_uid=24964761).

INTRODUCTION AND HYPOTHESIS: To evaluate an association between hysterectomy and urinary incontinence (UI) in postmenopausal women. METHODS: Women (aged 50-79) with uteri (N = 53,569) and without uteri (N = 38,524) who enrolled in the Women's Health Initiative (WHI) Observational Study between 1993 and 1996 were included in this secondary analysis. Baseline (BL) and 3-year demographic, health/physical forms and personal habit questionnaires were used. Statistical analyses included univariate and logistic regression methods. RESULTS: The baseline UI rate was 66.5 %, with 27.3 % of participants having stress urinary incontinence (SUI), 23 % having urge UI (UUI), and 12.4 % having mixed UI (MUI). 41.8 % of women had undergone hysterectomy, with 88.1 % having had the procedure before age 54. Controlling for health/physical variables, hysterectomy was associated with UI at BL (OR 1.25, 95 % CI 1.19, 1.32) and over the 3-year study period (OR 1.23, 95 % CI 1.11, 1.36). Excluding women with UI at BL, a higher incidence of UUI and SUI episodes was found in hysterectomy at year 3. Among women who had undergone hysterectomy, those with bilateral oophorectomy (BSO) did not have increased odds of developing UI at BL or over the 3-year study period. Hormone use was not associated with a change in UI incidence (estrogen + progesterone, p = 0.17; unopposed estrogen, p = 0.41). CONCLUSIONS: Risk of UI is increased in postmenopausal women who had undergone hysterectomy compared with women with uteri.

[**Eur J Clin Nutr.**](http://www.ncbi.nlm.nih.gov/pubmed/24961545)**2014 Jun 25. doi: 10.1038/ejcn.2014.117. [Epub ahead of print]**

**Sarcopenia, sarcopenic obesity and mortality in older adults: results from the National Health and Nutrition Examination Survey III.**

[Batsis JA](http://www.ncbi.nlm.nih.gov/pubmed?term=Batsis%20JA%5BAuthor%5D&cauthor=true&cauthor_uid=24961545)1, [Mackenzie TA](http://www.ncbi.nlm.nih.gov/pubmed?term=Mackenzie%20TA%5BAuthor%5D&cauthor=true&cauthor_uid=24961545)2, [Barre LK](http://www.ncbi.nlm.nih.gov/pubmed?term=Barre%20LK%5BAuthor%5D&cauthor=true&cauthor_uid=24961545)3, [Lopez-Jimenez F](http://www.ncbi.nlm.nih.gov/pubmed?term=Lopez-Jimenez%20F%5BAuthor%5D&cauthor=true&cauthor_uid=24961545)4, [Bartels SJ](http://www.ncbi.nlm.nih.gov/pubmed?term=Bartels%20SJ%5BAuthor%5D&cauthor=true&cauthor_uid=24961545)3.

Background:Sarcopenia is defined as the loss of skeletal muscle mass and quality, which accelerates with aging and is associated with functional decline. Rising obesity prevalence has led to a high-risk group with both disorders. We assessed mortality risk associated with sarcopenia and sarcopenic obesity in elders.Methods:A subsample of 4652 subjects ⩾60 years of age was identified from the National Health and Nutrition Examination Survey III (1988-1994), a cross-sectional survey of non-institutionalized adults. National Death Index data were linked to this data set. Sarcopenia was defined using a bioelectrical impedance formula validated using magnetic resonance imaging-measured skeletal mass by Janssen et al. Cutoffs for total skeletal muscle mass adjusted for height2 were sex-specific (men: ⩽5.75 kg/m2; females ⩽10.75 kg/m2). Obesity was based on % body fat (males: ⩾27%, females: ⩾38%). Modeling assessed mortality adjusting for age, sex, ethnicity (model 1), comorbidities (hypertension, diabetes, congestive heart failure,osteoporosis, cancer, coronary artery disease and arthritis), smoking, physical activity, self-reported health (model 2) and mobility limitations (model 3).Results:Mean age was 70.6±0.2 years and 57.2% were female. Median follow-up was 14.3 years (interquartile range: 12.5-16.1). Overall prevalence of sarcopenia was 35.4% in women and 75.5% in men, which increased with age. Prevalence of obesity was 60.8% in women and 54.4% in men. Sarcopenic obesity prevalence was 18.1% in women and 42.9% in men. There were 2782 (61.7%) deaths, of which 39.0% were cardiovascular. Women with sarcopenia and sarcopenic obesity had a higher mortality risk than those without sarcopenia or obesity after adjustment (model 2, hazard ratio (HR): 1.35 (1.05-1.74) and 1.29 (1.03-1.60)). After adjusting for mobility limitations (model 3), sarcopenia alone (HR: 1.32 ((1.04-1.69) but not sarcopenia with obesity (HR: 1.25 (0.99-1.58)) was associated with mortality. For men, the risk of death with sarcopenia and sarcopenic obesity was nonsignificant in both model-2 (HR: 0.98 (0.77-1.25), and HR: 0.99 (0.79-1.23)) and model 3 (HR: 0.98 (0.77-1.24) and HR: 0.98 (0.79-1.22)).Conclusions:Older women with sarcopenia have an increased all-cause mortality risk independent of obesity.

[**Cochrane Database Syst Rev.**](http://www.ncbi.nlm.nih.gov/pubmed/24960023)**2014 Jun 24;6:CD006033. [Epub ahead of print]**

**Steroidal contraceptives: effect on bone fractures in women.**

[Lopez LM](http://www.ncbi.nlm.nih.gov/pubmed?term=Lopez%20LM%5BAuthor%5D&cauthor=true&cauthor_uid=24960023)1, [Grimes DA](http://www.ncbi.nlm.nih.gov/pubmed?term=Grimes%20DA%5BAuthor%5D&cauthor=true&cauthor_uid=24960023), [Schulz KF](http://www.ncbi.nlm.nih.gov/pubmed?term=Schulz%20KF%5BAuthor%5D&cauthor=true&cauthor_uid=24960023), [Curtis KM](http://www.ncbi.nlm.nih.gov/pubmed?term=Curtis%20KM%5BAuthor%5D&cauthor=true&cauthor_uid=24960023), [Chen M](http://www.ncbi.nlm.nih.gov/pubmed?term=Chen%20M%5BAuthor%5D&cauthor=true&cauthor_uid=24960023).

Steroidal contraceptive use has been associated with changes in bone mineral density in women. Whether such changes increase the risk of fractures later in life is not clear. OBJECTIVES: Our aim was to evaluate the effect of using hormonal contraceptives beforemenopause on the risk of fracture in women. SEARCH METHODS: Through April 2014, we searched for studies of fracture or bone health and hormonal contraceptives in MEDLINE, POPLINE, CENTRAL, EMBASE, and LILACS, as well as ClinicalTrials.gov and ICTRP. Eligible interventions included comparisons of a hormonal contraceptive with a placebo or with another hormonal contraceptive that differed in terms of drug, dosage, or regimen. MAIN RESULTS: We found 19 RCTs that met our eligibility criteria. Eleven trials compared different combined oral contraceptives (COCs) or regimens of COCs; five examined an injectable versus another injectable, implant, or IUD; two studied implants, and one compared the transdermal patch versus the vaginal ring. No trial had fracture as an outcome. BMD was measured in 17 studies and 12 trials assessed biochemical markers of bone turnover. Depot medroxyprogesterone acetate (DMPA) was associated with decreased bone mineral density (BMD). The placebo-controlled trials showed BMD increases for DMPA plus estrogen supplement and decreases for DMPA plus placebo supplement. COCs did not appear to negatively affect BMD, and some formulations had more positive effects than others. However, no COC trial was placebo-controlled. Where studies showed differences between groups in bone turnover markers, the results were generally consistent with those for BMD. For implants, the single-rod etonogestrel group showed a greater BMD decrease versus the two-rod levonorgestrel group but results were not consistent across all implant comparisons.The sensitivity analysis included 11 trials providing evidence of moderate or high quality. Four trials involving DMPA showed some positive effects of an estrogen supplement on BMD, a negative effect of DMPA-subcutaneous on lumbar spine BMD, and a negative effect of DMPA on a bone formation marker. Of the three COC trials, one had a BMD decrease for the group with gestodene plus EE 15 μg. Another indicated less bone resorption in the group with gestodene plus EE 30 μg versus EE 20 μg. AUTHORS' CONCLUSIONS: Whether steroidal contraceptives influence fracture risk cannot be determined from existing information. The evidence quality was considered moderate overall, largely due to the trials of DMPA, implants, and the patch versus ring. The COC evidence varied in quality but was low overall. Many trials had small numbers of participants and some had large losses. Health care providers and women should consider the costs and benefits of these effective contraceptives. For example, injectable contraceptives and implants provide effective, long-term birth control yet do not involve a daily regimen. Progestin-only contraceptives are considered appropriate for women who should avoid estrogen due to medical conditions.