



Selección de Resúmenes de Menopausia

Semana del 17 al 23 de Abril de 2019

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Ann Intern Med. 2019 Apr 23. doi: 10.7326/M19-0533. [Epub ahead of print]

Long-Term Drug Therapy and Drug Discontinuations and Holidays for Osteoporosis Fracture Prevention: A Systematic Review.

Fink HA, MacDonald R, Forte ML, Rosebush CE, Ensrud KE, Schousboe JT, Nelson VA, Ullman K, Butler M, Olson CM, Taylor BC, Brasure M, Wilt TJ.

Background: Optimal long-term osteoporosis drug treatment (ODT) is uncertain. **Purpose:** To summarize the effects of long-term ODT and ODT discontinuation and holidays. **Data Sources:** Electronic bibliographic databases (January 1995 to October 2018) and systematic review bibliographies. **Study Selection:** 48 studies that enrolled men or postmenopausal women aged 50 years or older who were being investigated or treated for fracture prevention, compared long-term ODT (>3 years) versus control or ODT continuation versus discontinuation, reported incident fractures (for trials) or harms (for trials and observational studies), and had low or medium risk of bias (ROB). **Data Extraction:** Two reviewers independently rated ROB and strength of evidence (SOE). One extracted data; another verified accuracy. **Data Synthesis:** Thirty-five trials (9 unique studies) and 13 observational studies (11 unique studies) had low or medium ROB. In women with osteoporosis, 4 years of alendronate reduced clinical fractures (hazard ratio [HR], 0.64 [95% CI, 0.50 to 0.82]) and radiographic vertebral fractures (both moderate SOE), whereas 4 years of raloxifene reduced vertebral but not nonvertebral fractures. In women with osteopenia or osteoporosis, 6 years of zoledronic acid reduced clinical fractures (HR, 0.73 [CI, 0.60 to 0.90]), including nonvertebral fractures (high SOE) and clinical vertebral fractures (moderate SOE). Long-term bisphosphonates increased risk for 2 rare harms: atypical femoral fractures (low SOE) and osteonecrosis of the jaw (mostly low SOE). In women with unspecified osteoporosis status, 5 to 7 years of hormone therapy reduced clinical fractures (high SOE), including hip fractures (moderate SOE), but increased serious harms. After 3 to 5 years of treatment, bisphosphonate continuation versus discontinuation reduced radiographic vertebral fractures (zoledronic acid; low SOE) and clinical vertebral fractures (alendronate; moderate SOE) but not nonvertebral fractures (low SOE). **Limitation:** No trials studied men, clinical fracture data were sparse, methods for estimating harms were heterogeneous, and no trials compared sequential treatments or different durations of drug holidays. **Conclusion:** Long-term alendronate and zoledronic acid therapies reduce fracture risk in women with osteoporosis. Long-term bisphosphonate treatment may increase risk for rare adverse events, and continuing treatment beyond 3 to 5 years may reduce risk for vertebral fractures. Long-term hormone therapy reduces hip fracture risks but has serious harms.

Eur J Obstet Gynecol Reprod Biol. 2019 Apr 15;237:48-56. doi: 10.1016/j.ejogrb.2019.04.009. [Epub ahead of print]

The risk of malignancy in uterine polyps: A systematic review and meta-analysis.

Uglietti A, Buggio L, Farella M, Chiaffarino F, Dridi D, Vercellini P, Parazzini F.

BACKGROUND: Endometrial polyps are a common condition. The risk of malignancy has often led to an overtreatment with high health care costs and huge psychological distress. **OBJECTIVE:** We conducted a systematic review and a meta-analysis in order to estimate the prevalence of premalignant and malignant lesions in women undergoing hysteroscopic polypectomy. **DATA SOURCE:** We developed the search using PubMed/MEDLINE and EMBASE databases to identify papers published between 2000- January 2019. The research strategy used on Pubmed was: ("polyps" (MESH) OR "endometrial polyp*") AND ("malignancy" OR "cancer" OR "histopathology" OR "hysteroscopy" OR "ultrasound", OR "sonohysterography"). The same search was modified for EMBASE. **STUDY ELIGIBILITY:** We included all observational retrospective and prospective studies and studies were selected for the review if they met following inclusion criteria: pre-operative diagnosis of benign-looking endometrial polyps at ultrasound examination or at hysteroscopy, excision of endometrial polyps via surgical hysteroscopy, histopathological diagnosis of benign polyps, or hyperplasia without atypia, or premalignancy (atypical hyperplasia) or malignancy (endometrial cancer). Moreover, studies were included if number or percentage of subjects with and without malignancy was provided and if they reported data about menopausal and/or bleeding

status. We excluded data presented exclusively as abstracts in national and international meetings, or case report or review articles that did not include original data and papers published in other than English language. Our primary outcome was the prevalence of endometrial premalignant or malignant polyps in the total series, among premenopausal and postmenopausal women and among women with or without abnormal bleeding and then in subgroup analysis according to study design, diagnostic method, study region and calendar year of publication. RESULTS: A total of 51 studies reporting data on 35,345 women were included in this review. The prevalence of malignant polyps was 2.73% (95% CI 2.57-2.91) with very high heterogeneity among studies. The rates were lower for premenopausal women (1.12%) than post-menopausal ones (4.93%) and the difference was statistically significant (chi-square = 397.21. $p < .0001$). The risk of malignancy was higher among symptomatic (5.14%) than asymptomatic ones (1.89%) (chi-square = 133.13 $p < .001$). We observed higher rate of malignant polyps in prospective studies. In the meta-analysis selecting 10 prospective studies the random pooled estimate was 5.88 (95% CI: 4.06-7.97) with heterogeneity among studies (heterogeneity chi square = 17.55 $P = .025$) whereas in retrospective studies the random pooled estimate was 2.94 (95% CI: 2.24-3.71) with high heterogeneity among studies ($P < .001$). This finding can be due to more strict diagnostic criteria in prospective studies. CONCLUSION: Symptomatic vaginal bleeding and postmenopausal status in women with endometrial polyps increased the risk of malignancy. This finding could be an useful evidence to select patients who need to undergo hysteroscopic resection of endometrial polyps and women to whom, instead, an expectant management can be offer.

J Neurol Neurosurg Psychiatry Res. 2019 Jan-Jun;1(1). pii: 103. doi: 10.31531/edwiser.jnnpr.1000103. Epub 2019 Apr 1.

Women on Hormone Therapy with Ischemic Stroke, Effects on Deficits and Recovery.

Brown A, Wells J, Onteddu S, Bryant-Smith G, Sharma R, Joiner R, Nalleballe K, Richard-Davis G, Sheng S, et al. Hormone replacement therapy (HT) for post-menopausal women is associated with increased incidence of ischemic stroke risk. Effects of HT on stroke related deficits and functional outcomes in acute ischemic stroke (AIS) are uncertain. We retrospectively examined female consult data for HT use and National Institutes of Health Stroke Score (NIHSS) at baseline and recovery for 2015 and 2016 in a large stroke telemedicine program. Hypothesis: The age of women who acknowledged HT use will negatively impact stroke severity and outcomes. Methods: We analyzed consult data from two consecutive years for all women and included HT use, current age, and baseline and 24 h NIHSS's. We included all women consults regardless of IV Alteplase treatment. 24 h NIHSS and three month modified Rankin scale (mRS) were included from women given IV Alteplase. Results: Strokes were identified in 523 women and 244 women received Alteplase therapy. Women without HT use numbered 459 and 64 women listed HT use. Mean NIHSS scores regardless of HT use significantly improved 24 h NIHSS vs. baseline NIHSS ($p < 0.0001$). Baseline NIHSS scores were significantly improved in women on HT vs. non-HT users ($p = 0.01$) in women age 50 to 79 years. Although mean NIHSS scores at 24h was not different from HT to no HT use (4.9 ± 1.6 vs. 7.8 ± 0.6 , $p = 0.08$) a trend was present for lower NIHSS scores for women 50-79 years. The mRS scores at three months indicated significant improvements among HT users vs. non-HT use (1.46 ± 0.4 vs. 2.51 ± 0.2 , $p = 0.05$). Conclusion: While cautions persist on the use, route and dosage of HT for risks of ischemic stroke, the HT moderation of AIS deficits and outcomes in women < 80 years of age warrants further investigation.

Gynecol Endocrinol. 2019 Apr 22:1-5. doi: 10.1080/09513590.2019.1604656. [Epub ahead of print]

Risk factors associated with coronary artery calcification in midlife women: a population-based study.

Oppermann K, Colpani V, Spritzer PM.

The aim of this study was to investigate the association between individual risk factors and coronary artery calcification (CAC), as a marker of subclinical cardiovascular disease, in a population-based nested cross-sectional study of midlife women. Anthropometric and metabolic data from 295 women from the South of Brazil were analyzed. Habitual physical activity was assessed by pedometer. CAC was assessed by a multi-detector computed tomography system. Average Agatston score was used to stratify participants as $CAC > 0$ and $CAC = 0$. Women with $CAC > 0$ (34.7%) were older (58.7 ± 5.4 vs. 56.3 ± 5.2 years, $p < .001$) and had higher prevalence of central adiposity (71 vs. 59%, $p = .04$) and hypertension (71 vs. 52%, $p = .002$) than women in the $CAC = 0$ group. Hormone therapy (HT) was more prevalent in the group with $CAC = 0$ (19.7 vs. 9.8%, $p = .029$). The prevalence ratios for $CAC > 0$

were 0.545 (95%CI:0.309-0.962, $p = .036$) for HT and 1.752 (95%CI:1.207-2.541, $p = .003$) for hypertension, after adjustment for age, educational level, smoking, alcohol intake, and physical activity. The present data in a population-based sample of midlife women indicate that hypertension and age were positively associated with higher risk for CAC > 0 and HT was related with CAC = 0.

Horm Cancer. 2019 Apr 18. doi: 10.1007/s12672-019-00363-4. [Epub ahead of print]

Cabergoline Withdrawal Before and After Menopause: Outcomes in Microprolactinomas.

Indirli R, Ferrante E, Sala E, Giavoli C, Mantovani G, Arosio M.

Natural course of prolactinomas after menopause is not fully elucidated. The aim of this study was to compare recurrence rate after cabergoline withdrawal in premenopausal vs. postmenopausal women with microprolactinoma. Sixty-two women with microprolactinoma treated with cabergoline for at least 1 year and followed for 2 years after drug withdrawal were retrospectively selected. Patients were divided into two groups: 48 patients stopped cabergoline before menopause ("PRE" group), while 14 after menopause ("POST" group). Recurrence was defined by prolactin levels above normal, confirmed on two occasions. Overall, 39/62 women relapsed. Patients who relapsed apparently had higher prolactin before withdrawal (median 216.2, range 21.2-464.3 mIU/L) compared with those in long-term remission (94.3, 29.7-402.8 mIU/L; $p < 0.05$), and the risk of recurrence seemed lower in POST women (4/14, 29%) than in PRE ones (35/48, 73%, $p < 0.005$, OR 0.149, 95% CI 0.040-0.558). However, none of the factors (prolactin before withdrawal, menopausal status, treatment duration, complete adenoma regression) showed a correlation with recurrence risk in multivariate analysis. The best strategy able to optimize CBG treatment and withdrawal's outcomes is still to be defined in microprolactinomas. Postmenopausal status cannot reliably predict long-term remission, and follow-up is needed also in women of this age.

Ann Surg. 2019 Apr 13. doi: 10.1097/SLA.0000000000003331. [Epub ahead of print]

Bariatric Surgery is Associated With Reduced Risk of Breast Cancer in Both Premenopausal and Postmenopausal Women.

Feigelson HS, Caan B, Weinmann S, Leonard AC, Powers JD, Yenumula PR, Arterburn DE, Koebnick C, et al.

MINI: We examined risk of breast cancer among 17,998 women who had bariatric surgery and 53,889 women matched on body mass index with no surgery. We found bariatric surgery was associated with a reduced risk of both premenopausal [hazard ratio (HR) = 0.72, 95% confidence interval (CI), 0.54-0.94] and postmenopausal (HR = 0.55, 95% CI, 0.42-0.72) breast cancer. OBJECTIVE: This retrospective cohort study examined whether bariatric surgery is associated with reduced risk of breast cancer among pre- and postmenopausal women. BACKGROUND: Obesity is associated with increased risk of breast cancer, but the impact of weight loss on breast cancer risk has been difficult to quantify. METHODS: The cohort included obese (body mass index ≥ 35 kg/m²) patients enrolled in an integrated health care delivery system between 2005 and 2012 (with follow-up through 2014). Female bariatric surgery patients (N = 17,998) were matched on body mass index, age, study site, and comorbidity index to 53,889 women with no bariatric surgery. Kaplan-Meier curves and Cox proportional hazards models were used to examine incident breast cancer up to 10 years after bariatric surgery. Pre- and postmenopausal women were examined separately, and further classified by estrogen receptor (ER) status. RESULTS: The analysis included 301 premenopausal and 399 postmenopausal breast cancer cases. In multivariable adjusted models, bariatric surgery was associated with a reduced risk of both premenopausal (HR = 0.72, 95% CI, 0.54-0.94) and postmenopausal (HR = 0.55, 95% CI, 0.42-0.72) breast cancer. Among premenopausal women, the effect of bariatric surgery was more pronounced among ER-negative cases (HR = 0.36, 95% CI, 0.16-0.79). Among postmenopausal women, the effect was more pronounced in ER-positive cases (HR = 0.52, 95% CI, 0.39-0.70). CONCLUSIONS: Bariatric surgery was associated with a reduced risk of breast cancer among severely obese women. These findings have significant public health relevance because the prevalence of obesity continues to rise, and few modifiable breast cancer risk factors have been identified, especially for premenopausal women.

Eur J Sport Sci. 2019 Apr 18:1-10. doi: 10.1080/17461391.2019.1600588. [Epub ahead of print]

Substitution of sedentary time with light physical activity is related to increased bone density in U.S. women over 50 years old. An iso-temporal

substitution analysis based on the National health and Nutrition Examination Survey.

Ricci C, Gervasi F, Havemann Nel I, Smuts CM, Kruger SH, Leitzmann MF.

U.S. women are ageing. This is causing rises in osteoporosis prevalence and risk of fracture with related increases in health care costs. Replacing sedentary time with light physical activity may represent a cost effective public health solution to osteoporosis in elderly women. The National Health and Nutrition Examination Survey conducted over the period 2003-2006 provided cross-sectional data on bone mineral density and objectively assessed physical activity among 1,052 women aged 50-85 years old. Substitution analysis was applied to estimate increased bone mineral density and reduced osteoporosis for those women replacing 30 min of sedentary time with an equivalent amount of light physical activity. Substitution of 30 min of sedentary time with an equal amount of light physical activity was associated with increased bone mineral density of about 3 mg/cm² and a 12% reduced risk of osteoporosis in the spine. When considering overweight women and women over 65 years of age, this association was reinforced and it extended to the pelvis, legs and trunk, resulting in a consistent bone mineral density increase of about 3-6 mg/cm². The substitution of 30 min of sedentary time with an equal amount of light physical activity appears a possible primary prevention method to reduce osteoporosis and related increases in risk of fracture, mortality, and health care costs in women over 50 years old.