Selección de Resúmenes de Menopausia

Semana del 5 al 11 de diciembre de 2018

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PLoS One. 2018 Dec 6;13(12):e0208251. doi: 10.1371/journal.pone.0208251. eCollection 2018.

Screening for osteoporosis: A systematic assessment of the quality and content of clinical practice guidelines, using the AGREE II instrument and the IOM Standards for Trustworthy Guidelines.

Hayawi LM, Graham ID, Tugwell P, Yousef Abdelrazeq S.

BACKGROUND: Numerous clinical practice guidelines (CPGs) are published to guide management of osteoporosis. Little is known about their quality or how recommendations have changed over time. OBJECTIVE: To systematically assess the quality and content of the guidelines on screening for osteoporosis, using the Appraisal of Guidelines for Research and Evaluation (AGREE II) tool, and the Institute of Medicine (IOM) standards for trustworthy guidelines. METHODS: We conducted a systematic search for osteoporosis CPGs published between 2002-2016, using multiple databases and guideline websites. Two reviewers appraised the quality of eligible CPGs using the AGREE II. High quality CPGs were considered if they scored ≥ 60 in four or more domains including the domain for rigor of development. Non-parametric tests were used to test for the change of quality over time. One reviewer assessed the guidelines with IOM standards. We summarized the different evidence grading systems and extracted and compared the recommendations. RESULTS: A total of 33 CPGs were identified. The mean scores for AGREE II differed by domain (range: 42% to 71%). CPGs scored higher on domains for clarity of presentation, scope and purpose, and rigor of development. CPGs scored lower on domains for stakeholder involvement, editorial independence and applicability. Assessment of CPGs by IOM standards showed that CPGs scored better on standards for systematic review, establishing evidence foundation and rating strength of recommendation, articulation of recommendation, and establishing transparency. While scored lower on standards for updating, external review, and the development group composition. There was no difference in AGREE II and IOM defined guidelines' quality before and after the introduction of the two tools (P values >0.05). The IOM identified four more guidelines as high quality compared to the AGREE II. Examining these additional guidelines indicated that the two tools may give conflicting results especially for the rigor of development domain. Recommendations in certain areas showed substantial differences between guidelines. CONCLUSION: Osteoporosis screening CPGs are of variable quality, and their recommendations often differ. Guideline quality as measured by AGREE II and IOM standards has not improved overtime. Guideline developers should work together to improve the quality and consistency of recommendations to improve the likelihood that their guidelines will be used in practice.

Acta Med Port. 2018 Nov 30;31(11):680-690. doi: 10.20344/amp.9277. Epub 2018 Nov 30.

The Role of Testosterone in the Improvement of Sexual Desire in Postmenopausal Women: An Evidence-Based Clinical Review.

Gouveia M, Sanches R, Andrade S, Carmona S, Ferreira C.

INTRODUCTION: Female sexual dysfunction is a common problem, affecting more than 1/3 of women during their lives. The aim of this review is to review the evidence for the effectiveness of testosterone in sexual dysfunction in postmenopausal women, particularly in the improvement of sexual desire. MATERIAL AND METHODS: The authors searched in international databases National Guidelines Clearinghouse, Guidelines Finder, Cochrane Library and MEDLINE/PubMed, for guidelines, systematic reviews, meta-analysis and randomized controlled trials, published between January 2005 and February 2017, using the MeSH terms 'testosterone', 'androgens', 'libido', 'sexual dysfunctions' and 'menopause'. RESULTS: From a pool of 506 articles, 11 were selected: three guidelines, one systematic review with meta-analysis and seven randomized controlled trials. The selected articles showed testosterone's efficacy on global sexual function and improvement of sexual desire in postmenopausal women, when both are used in monotherapy or in association with other hormones. No study showed changes in hepatic enzymes or serious adverse effects. DISCUSSION: The small sample size and short follow-up used in the included studies limits the ability to assess testosterone's long-term benefits and effects. CONCLUSION: At short-term, testosterone seems to improve sexual function in postmenopausal women, particularly sexual desire. Nevertheless, more studies with larger sample size and longer follow-up are needed to understand its long-term safety and effectiveness.

JAMA Oncol. 2018 Dec 6. doi: 10.1001/jamaoncol.2018.5327. [Epub ahead of print]

Association of Body Fat and Risk of Breast Cancer in Postmenopausal Women with Normal Body Mass Index: A Secondary Analysis of a Randomized Clinical Trial and Observational Study.

Iyengar NM, Arthur R, Manson JE, Chlebowski RT, Kroenke CH, Peterson L, Cheng TD, Feliciano EC, et al

Importance: Obesity is associated with an increased risk of breast cancer, including the estrogen receptor (ER)-positive subtype in postmenopausal women. Whether excess adiposity is associated with increased risk in women with a normal body mass index (BMI; calculated as weight in kilograms divided by height in meters squared) is unknown. Objective: To investigate the association between body fat and breast cancer risk in women with normal BMI. Design, Setting, and Participants: This ad hoc secondary analysis of the Women's Health Initiative (WHI) clinical trial and observational study cohorts was restricted to postmenopausal participants with a BMI ranging from 18.5 to 24.9. Women aged 50 to 79 years were enrolled from October 1, 1993, through December 31, 1998. Of these, 3460 participants underwent body fat measurement with dual-energy x-ray absorptiometry (DXA) at 3 US designated centers with follow-up. At a median follow-up of 16 years (range, 9-20 years), 182 incident breast cancers had been ascertained, and 146 were ER positive. Follow-up was complete on September 30, 2016, and data from October 1, 1993, through September 30, 2016, was analyzed August 2, 2017, through August 21, 2018. Main Outcomes and Measures: Body fat levels were measured at baseline and years 1, 3, 6, and 9 using DXA. Information on demographic data, medical history, and lifestyle factors was collected at baseline. Invasive breast cancers were confirmed via central review of medical records by physician adjudicators. Blood analyte levels were measured in subsets of participants. Results: Among the 3460 women included in the analysis (mean [SD] age, 63.6 [7.6] years), multivariable-adjusted hazard ratios for the risk of invasive breast cancer were 1.89 (95% CI, 1.21-2.95) for the highest quartile of whole-body fat and 1.88 (95% CI, 1.18-2.98) for the highest quartile of trunk fat mass. The corresponding adjusted hazard ratios for ER-positive breast cancer were 2.21 (95% CI, 1.23-3.67) and 1.98 (95% CI, 1.18-3.31), respectively. Similar positive associations were observed for serial DXA measurements in time-dependent covariate analyses. Circulating levels of insulin, C-reactive protein, interleukin 6, leptin, and triglycerides were higher, whereas levels of high-density lipoprotein cholesterol and sex hormone-binding globulin were lower in those in the uppermost vs lowest quartiles of trunk fat mass. Conclusions and Relevance: In postmenopausal women with normal BMI, relatively high body fat levels were associated with an elevated risk of invasive breast cancer and altered levels of circulating metabolic and inflammatory factors. Normal BMI categorization may be an inadequate proxy for the risk of breast cancer in postmenopausal women.

Hum Reprod Update. 2018 Dec 1. doi: 10.1093/humupd/dmy039. [Epub ahead of print]

The route of administration, timing, duration and dose of postmenopausal hormone therapy and cardiovascular outcomes in women: a systematic review.

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BACKGROUND: The effect of postmenopausal hormone therapy (HT) on cardiovascular disease (CVD) risk remains controversial. OBJECTIVE AND RATIONALE: We aimed to systematically review the evidence regarding the role of dose, route of hormone administration, timing of initiation and duration of HT on cardiovascular risk among postmenopausal women. SEARCH METHODS: The electronic databases Medline Ovid, Web of Science and Cochrane Central were systematically searched to identify studies published before 30 January 2018. OUTCOMES: In total, 33 unique studies (6 trials and 27 prospective observational studies) were identified, including a total of 2 588 327 women. The synthesis of the existing knowledge on this topic was challenging due to inconsistent findings between some studies, caused by substantial diversity in scientific rigor and quality across the available literature. Overall, the evidence did not support the concerns that oral or transdermal HT increases heart disease risk. Contrary, observational data showed that a beneficial cardioprotective effect can be observed even with use of low doses of oral HT (effect of 0.3 mg/day of oral conjugated equine estrogen was similar to that seen with the standard dose of 0.625 mg/day), but clinical trials to support a cardioprotective benefit of HT in primary prevention have not been identified. Furthermore, the current data suggested that oral and transdermal HT, in dose-dependent manner and irrespective of HT formulation, may increase thromboembolic risk, as well as risk of stroke. However, transdermal estrogen with <50 μg/day of estrogen combined with micronized progesterone appears to be the safer choice with respect to thrombotic and stroke risk. Also, vaginal HT administration may play a role in myocardial infarction and stroke risk prevention, but this is based on limited evidence and requires further investigation. The timing of HT initiation and duration may be important factors to consider when prescribing HT especially in women with adverse cardiometabolic profile and pre-existing conditions such as coronary/carotid atherosclerosis, which are at risk of developing, and thus progressing to CVD. The

quality of evidence was generally low or moderate and the findings were based mostly on observational data. WIDER IMPLICATIONS: Use of low-dose oral and transdermal HT appears to be safe with regard to CVD risk in women in menopausal transition and within the first years (e.g. 10 years) after menopause onset. In women with increased baseline thromboembolic risk, alternative non-hormonal medications are suggested as first-line treatment and transdermal estradiol alone or with micronized progesterone only should be considered when these options are not effective. When HT is initiated >10 years since the menopause onset (>60 years old), due to greater absolute risks of coronary heart disease, stroke and venous thromboembolism, HT should be used for the shortest time possible and in lowest possible dose and preferably transdermal administration should be recommended. However, an individualized treatment approach including baseline CVD risk assessment should be applied when prescribing HT. The majority of studies included in the current review are from North American and European populations, which might limit the generalizability of the findings of this review to the other populations. Finally, the quality of evidence included in this review was generally low or moderate, highlighting a need for more rigorous research to help us better understand HT and cardiovascular health.

Anticancer Res. 2018 Dec;38(12):6615-6620. doi: 10.21873/anticanres.13028.

Does Transdermal Testosterone Increase the Risk of Developing Breast Cancer? A Systematic Review.

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BACKGROUND/AIM: Hypoactive sexual desire disorder (HSDD) is hypothesised to manifest in postmenopausal women at onset of menopause due to decreased oestrogen levels. Transdermal testosterone is a potential treatment option. This systematic review explores the relationship between the incidence of breast cancer and transdermal testosterone use. MATERIALS AND METHODS: Searches were conducted on the PubMed and Ovid databases. In Ovid, the advanced search function was used: 'transdermal testosterone not male'. In PubMed, the following search terms were used: 'transdermal, testosterone, menopausal, women, breast cancer, women'. Abstracts that fitted our initial criteria were further investigated. RESULTS: A total of 25 publications from PubMed and 192 publications from Ovid were initially assessed. Three randomised control trials were judged to have sufficiently met our inclusion criteria. However, these trials were too heterogeneous for a meta-analysis. A systematic review was deemed the most appropriate analysis of the data available. CONCLUSION: The publications examined in this systematic review suggest that the use of transdermal testosterone to treat HSDD in postmenopausal women does not increase breast cancer incidence. However, further research in the form of adequately powered randomised controlled trials with breast cancer incidence being the primary end point is required in order to confirm this.

Endocrine. 2018 Dec 4. doi: 10.1007/s12020-018-1824-9. [Epub ahead of print]

Use of antiosteoporotic drugs and calcium/vitamin D in patients with fragility fractures: impact on re-fracture and mortality risk.

Degli Esposti L, Girardi A, Saragoni S, Sella S, Andretta M, Rossini M, Giannini S; on the behalf of the Study

PURPOSE: To evaluate the impact of pharmacological treatment in osteoporosis patients with recent fracture and to assess the incidence of subsequent fracture and all-cause mortality. METHODS: This observational retrospective study was based on data from administrative databases of five Italian Local Health Units. Osteoporosis patients aged ≥ 50 years with hospitalization for vertebral or hip fracture occurring between 01/01/2011 and 31/12/2015 were included. Treatment adherence was calculated using the medication possession ratio. Multivariable proportional hazard Cox model was used to identify factors associated with time to re-fracture and all-cause mortality. RESULTS: A cohort of 3475 patients were included and 41.5% of them did not receive any specific anti-fracture treatment. Among treated patients (N = 2032), the majority (83.6%) received calcium/vitamin D supplementation. Over a mean follow-up of 3 years, the risk of subsequent fractures was 44.4% lower in treated patients compared to untreated ones (HR = 0.556, 95% CI = 0.420-0.735, p < 0.001) and 64.4% lower in those receiving calcium/vitamin D supplementation compared to osteoporosis treatment only (HR = 0.356, 95% CI = 0.237-0.533, p < 0.001). The risk of re-fracture was 77.2% lower in treated patients who were adherent to medication (HR = 0.228, 95% CI = 0.139-0.376, p < 0.001). Treated patients had 64% lower mortality risk over the follow-up compared to untreated ones (HR = 0.360, 95% CI = 0.310-0.418, p < 0.001). CONCLUSIONS: A consistent proportion of osteoporosis patients did not receive specific treatment after a fracture, showing poor adherence to national guidelines on osteoporosis treatment. Osteoporosis drug treatment, and

to a greater extent in combination with calcium/vitamin D, and adherence were correlated with lower risk of both re-fracture and all-cause mortality.

Maturitas. 2018 Nov 24. pii: S0378-5122(18)30742-4. doi: 10.1016/j. [Epub ahead of print]

Ospemifene for the treatment of vulvar and vaginal atrophy: A meta-analysis of randomized trials. Part I: Evaluation of efficacy.

Di Donato V, Schiavi MC, Iacobelli V, D'oria O, Kontopantelis E, Simoncini T, Muzii L, Benedetti Panici P.

OBJECTIVE: To evaluate the efficacy of ospemifene in treating dyspareunia associated with postmenopausal vulvo-vaginal atrophy (VVA). METHODS: A structured search was carried out in PubMed-Medlin, Embase, Cochrane Controlled Trials Register databases through to 31 July 2018. The search included the following terms: "Ospemifene", "vulvovaginal atrophy", "dyspareunia", "SERM" and "randomized controlled trial" (RCTs). Four outcomes were selected: vaginal pH; proportions of parabasal and superficial vaginal cells; and perception of the most bothersome symptom (vaginal dryness or dyspareunia). A random-effects model was used in the meta-analysis. Study quality and bias risk were assessed with the Cochrane tool. RESULTS: Six RCTs comparing the efficacy of ospemifene against placebo after 12 and 52 weeks of treatment were included in the meta-analysis. At 12 weeks, changes in vaginal Ph (SMD: -0.96, 95% CI:-1.12 to -0.81; $p < 0.0001$), parabasal cells (SMD: -36.84 95% CI -46.95 to -26.72; $p < 0.0001$), superficial cells (SMD: 8.23, 95% CI 3.73-12.74, $p < 0.0003$), and dyspareunia (SMD= - 2.70, 95% CI - 2.88 to -2.52, $p < 0.0001$) indicated that ospemifene was more effective than placebo. CONCLUSION: The present meta-analysis suggests that ospemifene 60 mg is associated with significant improvement in the morphological and physiological features of the vaginal mucosa that correlate with the symptoms associated with postmenopausal VVA.