



## Selección de Resúmenes de Menopausia

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María Soledad Vallejo. Clínica Quilín. Universidad de Chile

**Osteoporos Int. 2018 May 17. doi: 10.1007/s00198-018-4560-3. [Epub ahead of print]**

### Anti-osteoporosis drug use: too little, too much, or just right? The HUNT study, Norway.

Hoff M, Skurtveit S, Meyer HE, Langhammer A, Søgaard AJ, Syversen U, Skovlund E, Abrahamsen B, et al. Use of anti-osteoporotic drugs (AODs) was examined in a Norwegian population 50-85 year. Among them with Fracture Risk Assessment Tool (FRAX) score for major osteoporotic fracture  $\geq 20$ , 25% of the women and 17% of the men received AODs. The strongest predictors for AODs were high age in women and use of glucocorticoids among men. INTRODUCTION: To examine the use of anti-osteoporotic drugs (AODs) and to identify predictors for prescriptions. METHODS: Data were obtained from the Nord-Trøndelag Health Study (HUNT3) performed in 2006-2008 and the Norwegian Prescription Database, including 15,075 women and 13,386 men aged 50-85 years. Bone mineral density (BMD) in the femoral neck was measured in a subgroup of 4538 women and 2322 men. High fracture risk was defined as a FRAX score for major osteoporotic fracture (MOF)  $\geq 20\%$ ; in the subgroup with BMD, high risk was in addition defined as FRAXMOF  $\geq 20\%$  or T-score  $\leq -2.5$ . Hazard ratios (HRs) for predictors of incident use of AODs within 2 years after HUNT3 were estimated by Cox' proportional hazards model. RESULTS: Among individuals with FRAX MOF  $\geq 20\%$ , 25% of the women and 17% of the men were treated with AODs. Among those with FRAX MOF  $< 20\%$ , 3% and 1% were treated, respectively. In the subgroup with BMD measurement, 24% of the women and 16% of the men at high risk of fractures were treated, compared to 3 and 1% in women and men not fulfilling the criteria. In women, high age was the strongest predictor for treatment (HR 3.84: 95% confidence interval 2.81-5.24), followed by use of glucocorticoids (GCs) (2.68:1.84-3.89). In men, predictors were use of GCs (5.28: 2.70-10.35) followed by multimorbidity (3.16:1.31-7.63). In the subgroup with BMD, T-score  $\leq -2.5$  was the strongest predictor (women 3.98:2.67-5.89; men 13.31:6.17-28.74). CONCLUSIONS: This study suggests an undertreatment of AODs in individuals at high risk of fracture.

**J Cell Mol Med. 2018 May 16. doi: 10.1111/jcmm.13618. [Epub ahead of print]**

### Injection of synthetic mesenchymal stem cell mitigates osteoporosis in rats after ovariectomy.

Shen M, Wu R, Jin R, Pan J, Guo F, Li Z, Lin X, Xu S.

Osteoporosis is a severe skeletal disorder. Patients have a low bone mineral density and bone structural deterioration. Mounting lines of evidence suggest that inappropriate apoptosis of osteoblasts/osteocytes leads to maladaptive bone remodelling in osteoporosis. It has been suggested that transplantation of stem cells, including mesenchymal stem cells, may alter the trajectory of bone remoulding and mitigate osteoporosis in animal models. However, stem cells needed to be carefully stored and characterized before usage. In addition, there is great batch-to-batch variation in stem cell production. Here, we fabricated therapeutic polymer microparticles from the secretome and membranes of mesenchymal stem cells (MSCs). These synthetic MSCs contain growth factors secreted by MSCs. In addition, these particles display MSC surface molecules. In vitro, co-culture with synthetic MSCs increases the viability of osteoblast cells. In a rat model of ovariectomy-induced osteoporosis, injection of synthetic MSCs mitigated osteoporosis by reducing cell apoptosis and systemic inflammation, but increasing osteoblast numbers. Synthetic MSC offers a promising therapy to manage osteoporosis.

**Health Qual Life Outcomes. 2018 May 16;16(1):97. doi: 10.1186/s12955-018-0927-6.**

### Measuring bothersome menopausal symptoms: development and validation of the MenoScores questionnaire.

Lund KS, Siersma VD, Christensen KB, Waldorff FB, Brodersen J.

The experience of menopausal symptoms is common and an adequate patient-reported outcome measure is crucial in studies where women are treated for these symptoms. The aims of this study were to identify a patient-reported outcome measure for bothersome menopausal symptoms and, in the absence of an adequate tool, to develop a new measure with

high content validity, and to validate it using modern psychometric methods. METHODS: The literature was reviewed for existing questionnaires and checklists for bothersome menopausal symptoms. Relevant items were extracted and subsequently tested in group interviews, single interviews, and pilot tests. A patient-reported outcome measure was drafted and completed by 1504 women. Data was collected and psychometrically validated using item-response theory Rasch Models. RESULTS: All questionnaires identified in the literature lacked content validity regarding bothersome menopausal symptoms and none were validated using item-response theory. Our content validation resulted in a draft measurement encompassing 122 items across eight domains. Following psychometrical validation, the final version of our patient-reported outcome measure, named the MenoScores Questionnaire, encompassed 51 items, including one single item, covering 11 scales. CONCLUSION: Menopausal symptoms are multidimensional with some symptoms unquestionably related to the menopausal transition. We identified four constructs of importance: hot flushes, day-and-night sweats, general sweating, and menopausal-specific sleeping problems. The MenoScores Questionnaire is condition-specific with high content validity and adequate psychometrical properties. It is designed to measure bothersome menopausal symptoms and all scales are developed and psychometrically validated using item-response theory Rasch Models.

**PLoS One. 2018 May 16;13(5):e0197064. doi: 10.1371/journal.pone.0197064. eCollection 2018.**

### **Conjugated equine estrogen and medroxyprogesterone acetate are associated with decreased risk of breast cancer relative to bioidentical hormone therapy and controls.**

Zeng Z, Jiang X, Li X, Wells A, Luo Y, Neapolitan R.

OBJECTIVE: By the 1990s it became popular for women to use hormone therapy (HT) to ease menopause symptoms. Bioidentical estrogen and progesterone are supplements whose molecular structures are identical to what is made in the human body, while synthetic supplements are ones whose structures are not. After the Women's Health Initiative found that the combined use of the synthetics conjugated equine estrogen (CEE) and medroxyprogesterone acetate (MPA) increased breast cancer risk, prescriptions for synthetic HT declined considerably. Since then there has been an increased interest in bioidentical HT; today there are a plethora of websites touting their benefits. However, no peer-reviewed articles support these claims. We performed a retrospective study with the objective of verifying the hypothesis that bioidentical HT is associated with decreased breast cancer risk than CEE & MPA. METHODS: We searched The Northwestern Medicine Enterprise Data Warehouse for women who initiated HT use after age 50. Women who did not take any HT drug after age 50 served as controls. Nine HT protocols were investigated for breast cancer risk. RESULTS: Significant results include CEE Alone is associated with decreased breast cancer risk (HR = 0.31), Other Synthetic Estrogen Alone is associated with increased breast cancer risk (HR = 1.49), Bioidentical Estrogen Alone is associated with decreased breast cancer risk (HR = 0.65), CEE & MPA is associated with reduced breast cancer risk (HR = 0.43), and CEE & MPA is associated with reduced breast cancer risk relative to Bioidentical Estrogen & Progesterone (HR = 0.25). DISCUSSION: Our results indicate CEE & MPA is superior to bioidentical HT as far as breast cancer risk. Furthermore, this combination is associated with decrease of breast cancer risk, contrary to previous findings. Additional retrospective studies are needed to confirm our results.

**BMC Geriatr. 2018 May 15;18(1):115. doi: 10.1186/s12877-018-0809-0.**

### **Osteoporosis, diabetes, and hypertension are major risk factors for mortality in older adults: an intermediate report on a prospective survey of 1467 community-dwelling elderly healthy pensioners in Switzerland.**

Gutzwiller JP, Richterich JP, Stanga Z, Nydegger UE, Risch L, Risch M.

BACKGROUND: Osteoporosis is an important morbidity factor for ageing populations in developed countries. However, compared to the amount of information available on diabetes and cardiovascular disease, little is known about the direct impact of osteoporosis on general mortality in older age. METHODS: We obtained data from a prospective population-based cohort of pensioners from the SENIORLAB study who were subjectively healthy. The inclusion criteria were an age of at least 60 years and Swiss residence. We assessed and analysed clinical measures, voluntary reports, and laboratory values. RESULTS: In total, 1467 subjects were included in the cohort. The mean follow-up time was 3.68 years (95% confidence interval, 3.64-3.71). The ages of the included participants ranged from 60 to 99 years. At follow-up, there were 1401 survivors, and 66 participants had died. According to the multivariate analysis (Cox regression), osteoporosis was the most important risk factor for all-cause mortality (hazard ratio, 4.46; 95% confidence

interval, 1.82-10.91), followed by diabetes (hazard ratio, 2.17; 95% confidence interval, 1.04-4.52) and hypertension (hazard ratio, 1.81; 95% confidence interval, 1.09-3.03). CONCLUSIONS: Osteoporosis is a major risk factor for all-cause mortality in a subjectively healthy senior population, followed by type 2 diabetes mellitus and hypertension. Osteoporosis should be more actively diagnosed in healthy pensioners before they develop osteoporosis-associated health incidents.

**Cochrane Database Syst Rev. 2018 May 15;5:CD008830. doi: 10.1002/14651858. [Epub ahead of print]**

## **Hormone replacement therapy for women previously treated for endometrial cancer.**

Edey KA, Rundle S, Hickey M.

**BACKGROUND:** The majority of women diagnosed with endometrial cancer have early-stage disease, leading to a good prognosis after hysterectomy and removal of the ovaries (oophorectomy), with or without radiotherapy. Lack of oestrogen can cause hot flushes, night sweats, genital tract atrophy and longer-term adverse effects, such as osteoporosis and cardiovascular disease. Following bilateral oophorectomy, premenopausal women may develop significant and debilitating menopausal symptoms, so there is a need for information about the risk and benefits of taking HRT, enabling women to make an informed decision, weighing the advantages and disadvantages of using HRT for their individual circumstances. **OBJECTIVES:** To assess the risks and benefits of HRT (oestrogen alone or oestrogen with progestogen) for women previously treated for endometrial cancer. **SEARCH METHODS:** We searched the Cochrane Register of Controlled Trials (CENTRAL 2017, Issue 5), MEDLINE (1946 to April, week 4, 2017) and Embase (1980 to 2017, week 18). **SELECTION CRITERIA:** We included randomised controlled trials (RCTs), in all languages, that examined the efficacy of symptom relief and the safety of using HRT in women treated for endometrial cancer, where safety in this situation was considered as not increasing the risk of recurrence of endometrial cancer above that of women not taking HRT. **MAIN RESULTS:** This study reported tumour recurrence in 2.3% of women in the oestrogen arm versus 1.9% of women receiving placebo (risk ratio (RR) 1.17, 95% confidence interval (CI) 0.54 to 2.50; very low-certainty evidence). The study did not report on symptom relief, overall survival or progression-free survival for HRT versus placebo. However, they did report the percentage of women alive with no evidence of disease (94.3% in the HRT group and 95.6% in the placebo group) and the percentage of women alive irrespective of disease progression (95.8% in the HRT group and 96.9% in the placebo group) at the end of the 36 months' follow-up. The study did not report time to recurrence and it was underpowered due to closing early. **AUTHORS' CONCLUSIONS:** Currently, there is insufficient high-quality evidence to inform women considering HRT after treatment for endometrial cancer. The available evidence (both the single RCT and non-randomised evidence) does not suggest significant harm, if HRT is used after surgical treatment for early-stage endometrial cancer. There is no information available regarding use of HRT in higher-stage endometrial cancer (FIGO stage II and above). The use of HRT after endometrial cancer treatment should be individualised, taking account of the woman's symptoms and preferences, and the uncertainty of evidence for and against HRT use.

**Breast. 2018 May 12;40:123-130. doi: 10.1016/j.breast.2018.05.002. [Epub ahead of print]**

## **The oncologic impact of hormone replacement therapy in premenopausal breast cancer survivors: A systematic review.**

Wang Y, Lewin N, Qaoud Y, Rajaei AN, Scheer AS.

**SYNOPSIS:** This is the first systematic review to investigate the risk of recurrence in breast cancer survivors <50 years old who have used hormone replacement therapy (HRT). **BACKGROUND:** The risk of HRT in premenopausal breast cancer survivors is unclear. Due to the higher incidence of estrogen receptor negative tumours in women <50, the potential for HRT to promote breast cancer recurrence may differ from older age groups. **METHODS:** We performed a search of Medline, EMBASE and CINAHL through June 2016. For the observational studies relative risk (RR) and 95% confidence interval (CI) were calculated for the recurrence rate among HRT users and nonusers. A random effects model was used to estimate the combined RR using the Mantel-Haenszel method. **RESULTS:** Four papers satisfied our inclusion criteria. 3477 subjects were analyzed. On pooled meta-analysis of breast cancer recurrence in the observational studies, no significant association was found between HRT and risk of recurrence (RR 1.04 [95% CI 0.45, 2.41]). The randomized controlled trial (RCT) included found an increased risk of recurrence with HRT among women <50 (HR 1.56 [95% CI 1.1-2.2]). However, among women of all ages with an estrogen receptor negative tumour there was no significant difference in recurrence when compared to hormone receptor positive tumours (HR 1.15 [95% CI 0.7-1.8,

$p = 0.55$ ). DISCUSSION: This review on HRT in breast cancer survivors <50 revealed conflicting results between randomized and observational study data. Further studies are warranted to investigate the association between HRT and recurrence rates in younger breast cancer survivors.

**Menopause. 2018 May 14. doi: 10.1097/GME.0000000000001121. [Epub ahead of print]**

## **Management of genitourinary syndrome of menopause in women with or at high risk for breast cancer: consensus recommendations from The North American Menopause Society and The International Society for the Study of Women's Sexual Health.**

Faubion SS, Larkin LC, Stuenkel CA, Bachmann GA, Chism LA, Kagan R, Kaunitz AM, Krychman ML, et al.

The objective of The North American Menopause Society (NAMS) and The International Society for the Study of Women's Sexual Health (ISSWSH) Expert Consensus Panel was to create a point of care algorithm for treating genitourinary syndrome of menopause (GSM) in women with or at high risk for breast cancer. The consensus recommendations will assist healthcare providers in managing GSM with a goal of improving the care and quality of life for these women. The Expert Consensus Panel is comprised of a diverse group of 16 multidisciplinary experts well respected in their fields. The panelists individually conducted an evidence-based review of the literature in their respective areas of expertise. They then met to discuss the latest treatment options for genitourinary syndrome of menopause (GSM) in survivors of breast cancer and review management strategies for GSM in women with or at high risk for breast cancer, using a modified Delphi method. This iterative process involved presentations summarizing the current literature, debate, and discussion of divergent opinions concerning GSM assessment and management, leading to the development of consensus recommendations for the clinician. Genitourinary syndrome of menopause is more prevalent in survivors of breast cancer, is commonly undiagnosed and untreated, and may have early onset because of cancer treatments or risk-reducing strategies. The paucity of evidence regarding the safety of vaginal hormone therapies in women with or at high risk for breast cancer has resulted in avoidance of treatment, potentially adversely affecting quality of life and intimate relationships. Factors influencing decision-making regarding treatment for GSM include breast cancer recurrence risk, severity of symptoms, response to prior therapies, and personal preference. We review current evidence for various pharmacologic and nonpharmacologic therapeutic modalities in women with a history of or at high risk for breast cancer and highlight the substantial gaps in the evidence for safe and effective therapies and the need for future research. Treatment of GSM is individualized, with nonhormone treatments generally being first line in this population. The use of local hormone therapies may be an option for some women who fail nonpharmacologic and nonhormone treatments after a discussion of risks and benefits and review with a woman's oncologist. We provide consensus recommendations for an approach to the management of GSM in specific patient populations, including women at high risk for breast cancer, women with estrogen-receptor positive breast cancers, women with triple-negative breast cancers, and women with metastatic disease.

**BMC Musculoskelet Disord. 2018 May 14;19(1):144. doi: 10.1186/s12891-018-2060-4.**

## **Prevalence and comorbidity of osteoporosis- a cross-sectional analysis on 10,660 adults aged 50 years and older in Germany.**

Puth MT, Klaschik M, Schmid M, Weckbecker K, Münster E.

**BACKGROUND:** Knowledge on prevalence of osteoporosis stratifying for socioeconomic background is insufficient in Germany. Little is known in Europe about other diseases that go along with it although these aspects are important for implementing effective public health strategies. **METHODS:** This cross-sectional analysis was based on the national telephone survey "German Health Update" (GEDA 2012) performed in 2012/2013. GEDA 2012 provides information on self-reported diseases and sociodemographic characteristics for nearly 20,000 adults. Descriptive statistical analysis and multiple logistic regression were used to examine the association between osteoporosis and age, sex, other diseases and education defined by ISCED. Analyses were limited to participants aged 50 years and older. **RESULTS:** Overall, 8.7% of the 10,660 participants aged 50+ years had osteoporosis (men 4.7%, women 12.2%). More than 95% of the adults with osteoporosis had at least one coexisting disease. The odds for arthrosis (OR 3.3, 95% CI 2.6-4.1), arthritis (OR 3.0, 95% CI 2.2-4.2), chronic low back pain (OR 2.8, 95% CI 2.3-3.5), depression (OR 2.3, 95% CI 1.7-3.1) and chronic heart failure (OR 2.3, 95% CI 1.6-3.1), respectively, were greater for adults with osteoporosis. Education showed no significant association with osteoporosis. **CONCLUSIONS:** There was no clear evidence of socioeconomic differences regarding osteoporosis for adults in Germany. However, clinicians need to be aware that multimorbidity is very common in adults with osteoporosis. Health care interventions for osteoporosis could be improved by offering

preventive care for other diseases that go along with it. Over- or under-diagnosis in different socioeconomic levels has to be further explored.