



## Selección de Resúmenes de Menopausia

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### Reproductive period and risk of dementia in a diverse cohort of health care members.

Gilsanz P, Lee C, Corrada MM, Kawas CH, Quesenberry CP Jr, Whitmer RA.

**OBJECTIVE:** Women have >50% greater lifetime risk of dementia than men but the role of female-specific endocrine milieu is not well-understood. This study evaluates associations between indicators of estrogen exposure from women's reproductive period and dementia risk in a large diverse population. **METHODS:** We evaluated 15,754 female members (29.9% nonwhite) of Kaiser Permanente with clinical examinations and health survey data from 1964 to 1973 and were members as of January 1, 1996. In midlife (mean age 51.1 years), women reported age at menarche and menopause and hysterectomy status. Reproductive span was calculated as menopause age minus menarche age. Dementia diagnoses were abstracted from January 1, 1996 to September 30, 2017 medical records (mean age at start of dementia follow-up 76.5 years). Cox proportional hazard models evaluated associations between aspects of reproductive span and dementia risk adjusting for demographics and life course health indicators. **RESULTS:** Forty-two percent of women developed dementia. Compared to menarche at age 13.0 (mean menarche age), menarche at  $\geq 16$  was associated with 23% greater dementia risk (adjusted hazard ratio [HR] 1.23; 95% confidence interval [CI] 1.01-1.50) adjusting for demographics and life course health indicators. Natural menopause at age <47.4 (mean menopause age) was associated with 19% elevated dementia risk (HR 1.19; 95% CI 1.07-1.31). Reproductive spans <34.4 years (mean duration) were associated with 20% elevated dementia risk (HR 1.20; 95% CI 1.08-1.32). Hysterectomies were associated with 8% elevated dementia risk (HR 1.08; 95% CI 1.01-1.16). **CONCLUSION:** In this large prospective cohort study, endocrine events signaling less estradiol exposure (i.e., later age at menarche, younger age at menopause, shorter reproductive span, and hysterectomies) were associated with elevated risk of dementia.

**J Bone Miner Res. 2019 Mar 28. doi: 10.1002/jbmr.3717. [Epub ahead of print]**

### Performance of FRAX and FRAX-Based Treatment Thresholds in Women Aged 40 and Older: The Manitoba BMD Registry.

Crandall CJ, Schousboe JT, Morin SN, Lix LM, Leslie W.

We examined among women aged  $\geq 40$  years the performance of the Fracture Risk Assessment Tool (FRAX) and FRAX-based osteoporosis treatment thresholds under the U.S. National Osteoporosis Foundation (NOF) and U.K. National Osteoporosis Guideline Group (NOGG) guidelines. We used registry data for all women aged  $\geq 40$  years in Manitoba, Canada with baseline bone mineral density (BMD) testing ( $n = 54,459$ ). Incident major osteoporotic fracture (MOF), hip fracture, and clinical fracture were assessed from population-based health services data (mean follow-up 10.5 years). Age-stratified hazard ratios (HR) were estimated from Cox regression models. We assessed the sensitivity, specificity, positive predictive value (PPV), number needed to screen (NNS), and number needed to treat (NNT) to prevent a fracture (assuming 20% relative risk reduction on treatment) for osteoporosis treatment thresholds under the NOF and NOGG guidelines. Femoral neck T-score and FRAX (with and without BMD) predicted all fracture outcomes at all ages. There was good calibration in FRAX-predicted vs. observed 10-year MOF and hip fracture probability. Overall sensitivity (PPV) for incident MOF was: 25.7% (24.0%) for femoral neck T-score  $\leq -2.5$ , 20.3% (26.3%) for FRAX (with BMD)-predicted 10-year MOF risk  $\geq 20\%$  (NOF threshold), 27.3% (22.0%) for FRAX-predicted 10-year MOF risk  $\geq$  age-dependent cutoff (NOGG threshold), 59.4% (19.0%) for the NOF treatment algorithm, and 28.5% (18.4%) for the NOGG treatment algorithm. Sensitivity for identifying incident MOF varied by age, ranging from 0.0% - 26.3% in women 40-49 years-old and from 49.0% to 93.3% in women aged 80+. The gradient of risk for fracture prediction from femoral neck T-score and FRAX (with and without BMD) as continuous measures was strong across the age spectrum. The sensitivity and PPV of the strategies based on dichotomous cutoffs are low, especially among women aged 40-49 years (who have lowest incidence rates). Threshold-based approaches should be reassessed, particularly in younger women.

**Cancer Res Treat. 2019 Mar 21. doi: 10.4143/crt.2018.705. [Epub ahead of print]**

## **Television Viewing Time and Breast Cancer Incidence for Japanese Premenopausal and Postmenopausal Women: The JACC Study.**

Cao J, Eshak ES, Liu K, Muraki I, Cui R, Iso H, Tamakoshi A; JACC Study Group.

Purpose: The evidence on effects of TV viewing time among premenopausal and postmenopausal women for breast cancer risk remains controversial and limited. Materials and Methods: A prospective study encompassing 33,276 (17,568 premenopausal, and 15,708 postmenopausal) women aged 40-79 years in whom TV viewing time, menstrual and reproductive histories were determined by a self-administered questionnaire. The follow-up was from 1988 to 2009 and hazard ratios (HRs) with 95% confidence intervals (CIs) of breast cancer incidence were calculated for longer TV viewing time in reference to shorter TV viewing time by Cox proportional hazard models. Results: During 16.8-year median follow-up, we found positive associations between TV viewing time and breast cancer incidence with a borderline significant trend among total women and a significant trend among postmenopausal women. Among total women, the multivariable HRs (95% CIs) for risk of breast cancer in reference to < 1.5 hr/day of TV viewing time were 0.89 (0.59-1.34) for 1.5 to < 3.0 hr/day, 1.19 (0.82-1.74) for 3.0 to < 4.5 hr/day, and 1.45 (0.91-2.32) for  $\geq$  4.5 hr/day ( $p$  for trend=0.053) and among postmenopausal women, the corresponding risk estimates were 1.10 (0.42-2.88), 2.54 (1.11-5.80), and 2.37 (0.92-6.10) ( $p$  for trend=0.009), respectively. Conclusion: Prolonged TV viewing time was associated with increased risk of breast cancer, especially among postmenopausal women.

**Aging (Albany NY). 2019 Mar 25. doi: 10.18632/aging.101874. [Epub ahead of print]**

## **Muscle-derived miR-34a increases with age in circulating extracellular vesicles and induces senescence of bone marrow stem cells.**

Fulzele S, Mendhe B, Khayrullin A, Johnson M, Kaiser H, Liu Y, Isales CM, Hamrick MW.

Extracellular vesicles (EVs) are known to play important roles in cell-cell communication. Here we investigated the role of muscle-derived EVs and their microRNAs in the loss of bone stem cell populations with age. Aging in male and female C57BL6 mice was associated with a significant increase in expression of the senescence-associated microRNA miR-34a-5p (miR-34a) in skeletal muscle and in serum -derived EVs. Muscle-derived, alpha-sarcoglycan positive, EVs isolated from serum samples also showed a significant increase in miR-34a with age. EVs were isolated from conditioned medium of C2C12 mouse myoblasts and primary human myotubes after cells were treated with hydrogen peroxide to simulate oxidative stress. These EVs were shown to have elevated levels of miR-34a, and these EVs decreased viability of bone marrow mesenchymal (stromal) cells (BMSCs) and increased BMSC senescence. A lentiviral vector system was used to overexpress miR-34a in C2C12 cells, and EVs isolated from these transfected cells were observed to home to bone in vivo and to induce senescence and decrease Sirt1 expression of primary bone marrow cells ex vivo. These findings suggest that aged skeletal muscle is a potential source of circulating, senescence-associated EVs that may directly impact stem cell populations in tissues such as bone via their microRNA cargo.

**Nutr Health. 2019 Mar 26;260106019838365. doi: 10.1177/0260106019838365. [Epub ahead of print]**

## **Effects of higher habitual protein intake on resistance-training-induced changes in body composition and muscular strength in untrained older women: a clinical trial study.**

Nabuco HC, Tomeleri CM, Junior PS, Fernandes RR, Cavalcante EF, Nunes JP, Cunha PF, Dos Santos L, Cyrino ES.

BACKGROUND: Aging is accompanied by progressive and accentuated decline in muscular strength and skeletal muscle mass, affecting health and functional autonomy. Both resistance training (RT) and diet are strategies that may contribute to improvement in the health of the elderly. AIM: The purpose of this study was to evaluate the effects of higher habitual protein intake on RT-induced changes in body composition and strength in untrained postmenopausal women. METHODS: Seventy older women were submitted to an RT program. Body composition, muscular strength, and dietary intake (24 h dietary recall) were performed pre- and post-intervention. To verify different intervention effects according to protein intake of the participants, the sample was separated into tertiles according to protein intake: low, moderate, and high protein intake. RESULTS: A time vs. group interaction ( $p < 0.05$ ) was observed, with high protein intake presenting greater increases compared with low protein intake, for skeletal muscle mass

(5.3% vs. 1.3%), lower limb lean soft tissue (4.9% vs. 1.4%), upper lean soft tissue (4.9% vs. 1.2%), preacher curl (24% vs. 15.2%), and total strength (16.4% vs. 11.7%). A time vs. group interaction ( $p < 0.05$ ) was observed, with high protein intake presenting greater increases compared with moderate protein intake, for skeletal muscle mass (5.3% vs. 3.2%). In all groups, a main effect of time ( $p < 0.05$ ) was observed for knee extension and chest press. CONCLUSIONS: We conclude that intake of  $>1.0$  g/kg/day of protein promotes gains in skeletal muscle mass and muscular strength after RT in untrained older women.

**Crit Rev Food Sci Nutr. 2019 Mar 26:1-16. doi: 10.1080/10408398.2019.1590800. [Epub ahead of print]**

## **Consumption of milk and dairy products and risk of osteoporosis and hip fracture: a systematic review and Meta-analysis.**

Malmir H, Larijani B, Esmailzadeh A.

BACKGROUND: Although some studies have reported the beneficial effects of milk and dairy product consumption on osteoporosis and risk of fracture, the findings are conflicting. PURPOSE: We summarized earlier data on the association between milk and dairy intake and risk of osteoporosis and hip fracture through a meta-analysis. METHODS: A systematic literature search of relevant reports published in PubMed, ISI (Web of Science), EMBASE, SCOPUS, and Google Scholar until August 2018 was conducted. RESULTS: Total dairy intake was protectively associated with reduced risk of osteoporosis based on cross-sectional and case-control studies (0.63; 95% CI: 0.55-0.73). Milk consumption was not associated with the risk of osteoporosis (overall RR = 0.79; 95% CI: 0.57-1.08). In non-linear dose-response meta-analysis, increase intake of dairy (at the level of 0 to 250 grams per day) was associated with a reduced risk of osteoporosis ( $P_{\text{nonlinearity}} = 0.005$ ). Meta-regression of included studies revealed an inverse linear association between dairy and milk intake and risk of osteoporosis; such that every additional 200-gram intake of dairy and milk was associated with a 22% and 37% reduced risk of osteoporosis, respectively. In terms of hip fracture, milk consumption was associated with a 25% reduced risk of hip fracture only in cross-sectional and case-control studies (overall RR = 0.75; 95% CI: 0.57-0.99). In linear meta-regression, every additional 200-gram milk intake per day was associated with a 9% greater risk of hip fracture in cohort studies. CONCLUSION: Despite an inverse association between milk and dairy intake and risk of osteoporosis and hip fracture in cross-sectional and case-control studies, no such association was seen in cohort studies. Given the advantages of the cohort over case-control studies, we concluded that a greater intake of milk and dairy products was not associated with a lower risk of osteoporosis and hip fracture.