



Selección de Resúmenes de Menopausia

Semana del 11 al 17 de Febrero de 2015

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Alcohol intake and breast cancer in the European Prospective investigation into Cancer and Nutrition.

Romieu I, Scoccianti C, Chajes V, de Batlle J, Biessy C, Dossus L, Baglietto L, Clavel-Chapelon F, et al.

Alcohol intake has been associated to breast cancer in pre and postmenopausal women; however results are inconclusive regarding tumor hormonal receptor status, and potential modifying factors like age at start drinking. Therefore, we investigated the relation between alcohol intake and the risk of breast cancer using prospective observational data from the European Prospective Investigation into Cancer and Nutrition (EPIC). Up to 334,850 women, aged 35-70 years at baseline, were recruited in ten European countries and followed up an average of 11 years. Alcohol intake at baseline and average lifetime alcohol intake were calculated from country-specific dietary and lifestyle questionnaires. The study outcomes were the Hazard ratios (HR) of developing breast cancer according to hormonal receptor status. During 3,670,439 person-years, 11,576 incident breast cancer cases were diagnosed. Alcohol intake was significantly related to breast cancer risk, for each 10g/day increase in alcohol intake the HR increased by 4.2% (95% CI: 2.7%-5.8%). Taking 0 to 5g/day as reference, alcohol intake of >5 to 15g/day was related to a 5.9% increase in breast cancer risk (95% CI: 1%-11%). Significant increasing trends were observed between alcohol intake and ER+/PR+, ER-/PR-, HER2- and ER-/PR-/HER2- tumors. Breast cancer risk was stronger among women who started drinking prior to first full-time pregnancy. Overall, our results confirm the association between alcohol intake and both hormone receptor positive and hormone receptor negative breast tumors, suggesting that timing of exposure to alcohol drinking may affect the risk. Therefore, women should be advised to control their alcohol consumption.

Lancet. 2015 Feb 12. pii: S0140-6736(14)61687-1. doi: 10.1016/S0140-6736(14)61687-1. [Epub ahead of print]

Menopausal hormone use and ovarian cancer risk: individual participant meta-analysis of 52 epidemiological studies. Collaborative Group On Epidemiological Studies Of Ovarian Cancer.

BACKGROUND: Half the epidemiological studies with information about menopausal hormone therapy and ovarian cancer risk remain unpublished, and some retrospective studies could have been biased by selective participation or recall. We aimed to assess with minimal bias the effects of hormone therapy on ovarian cancer risk. **METHODS:** Individual participant datasets from 52 epidemiological studies were analysed centrally. The principal analyses involved the prospective studies (with last hormone therapy use extrapolated forwards for up to 4 years). Sensitivity analyses included the retrospective studies. Adjusted Poisson regressions yielded relative risks (RRs) versus never-use. **FINDINGS:** During prospective follow-up, 12 110 postmenopausal women, 55% (6601) of whom had used hormone therapy, developed ovarian cancer. Among women last recorded as current users, risk was increased even with <5 years of use (RR 1.43, 95% CI 1.31-1.56; $p < 0.0001$). Combining current-or-recent use (any duration, but stopped <5 years before diagnosis) resulted in an RR of 1.37 (95% CI 1.29-1.46; $p < 0.0001$); this risk was similar in European and American prospective studies and for oestrogen-only and oestrogen-progestagen preparations, but differed across the four main tumour types (heterogeneity $p < 0.0001$), being definitely increased only for the two most common types, serous (RR 1.53, 95% CI 1.40-1.66; $p < 0.0001$) and endometrioid (1.42, 1.20-1.67; $p < 0.0001$). Risk declined the longer ago use had ceased, although about 10 years after stopping long-duration hormone therapy use there was still an excess of serous or endometrioid tumours (RR 1.25, 95% CI 1.07-1.46, $p = 0.005$). **INTERPRETATION:** The increased risk may well be largely or wholly causal; if it is, women who use hormone therapy for 5 years from around age 50 years have about one extra ovarian cancer per 1000 users and, if its prognosis is typical, about one extra ovarian cancer death per 1700 users.

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Sex differences in cardiovascular risk factors and disease prevention.

Appelman Y, van Rijn BB, Ten Haaf ME, Boersma E, Peters SA.

Cardiovascular disease (CVD) has been seen as a men's disease for decades, however it is more common in women than in men. It is generally assumed in medicine that the effects of the major risk factors (RF) on CVD outcomes are the same in women as in men. Recent evidence has emerged that recognizes new, potentially independent, CVD RF exclusive to women. In particular, common disorders of pregnancy, such as gestational hypertension and diabetes, as well as frequently occurring endocrine disorders in women of reproductive age (e.g. polycystic ovary syndrome (PCOS) and early menopause) are associated with accelerated development of CVD and impaired CVD-free survival. With the recent availability of prospective studies comprising men and women, the equivalency of major RF prevalence and effects on CVD between men and women can be examined. Furthermore, female-specific RFs might be identified enabling early detection of apparently healthy women with a high lifetime risk of CVD. Therefore, we examined the available literature regarding the prevalence and effects of the traditional major RFs for CVD in men and women. This included large prospective cohort studies, cross-sectional studies and registries, as randomised trials are lacking. Furthermore, a literature search was performed to examine the impact of female-specific RFs on the traditional RFs and the occurrence of CVD. We found that the effects of elevated blood pressure, overweight and obesity, and elevated cholesterol on CVD outcomes are largely similar between women and men, however prolonged smoking is significantly more hazardous for women than for men. With respect to female-specific RF only associations (and no absolute risk data) could be found between preeclampsia, gestational diabetes and menopause onset with the occurrence of CVD. This review shows that CVD is the main cause of death in men and women, however the prevalence is higher in women. Determination of the CV risk profile should take into account that there are differences in impact of major CV RF leading to a worse outcome in women. Lifestyle interventions and awareness in women needs more consideration. Furthermore, there is accumulating evidence that female-specific RF are of influence on the impact of major RF and on the onset of CVD. Attention for female specific RF may enable early detection and intervention in apparently healthy women. Studies are needed on how to implement the added RF's in current risk assessment and management strategies to maximize benefit and cost-effectiveness specific in women.

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Effects of hormone replacement therapy on depressive and anxiety symptoms after oophorectomy.

Đoković DD, Jović JJ, Đoković JD, Knežević MŽ, Djukić-Dejanović S, Ristić-Ignjatović DI.

Aim To assess the effect of hormone replacement therapy on postoperative depression and anxiety symptoms. **Methods** In observational prospective study 80 women divided into two groups were evaluated: women who received estrogen and androgen replacement therapy after hysterectomy with bilateral oophorectomy before onset of menopause (35-45 years old) and a control group that consisted of perimenopausal women (45-55 years old). Hormone replacement therapy began one week after surgery. The severity of depression and anxiety was evaluated through the use of Hamilton Depression Rating Scale and Hamilton Anxiety Rating Scale. Subjects from the study group were interviewed right after the surgical treatment, one, two and three months later. Subjects from the control group were interviewed only once. **Results** The women who underwent surgery had a statistically significantly higher score in Hamilton Depression Scale (p less than 0.001) and Hamilton Anxiety Scale ($p=0.002$) compared to the control perimenopausal women. There was a significant reduction of depressive and anxiety symptoms during hormone replacement therapy. Statistically significant difference in depressive score was found immediately after one month of hormone replacement therapy (first week/one month later: $p=0.0057$). Statistically significant difference in anxiety score appeared three months after the introduction of hormone therapy (first week/one month later: $p=0.309$; first week/two months later: $p=0.046$; first week/three months later: p less than 0.001). Level of serum luteinizing hormone was in correlation with depressive and anxiety score. **Conclusion** Estrogen-androgen replacement therapy may reduce the risk of psychiatric disorders developing in women with bilateral oophorectomy (indication for hysterectomy with oophorectomy was leiomyomata uteri).

Menopause. 2015 Feb 9. [Epub ahead of print]

Waist circumference and postmenopause stages as the main associated factors for sleep apnea in women: a cross-sectional population-based study.

Polesel DN, Hirotsu C, Nozoe KT, Boin AC, Bittencourt L, Tufik S, Andersen ML, Hachul H.

OBJECTIVE: The current study aimed to investigate stages of reproductive aging as an associated factor for obstructive sleep apnea syndrome (OSAS) among women in a representative sample of Sao Paulo, Brazil. **METHODS:** Four hundred seven women underwent clinical evaluation, polysomnography, and biochemical analysis. Stages of reproductive aging were defined as premenopause, early postmenopause, and late postmenopause. **RESULTS:** OSAS was more frequent in the postmenopausal groups, with 68.4% of women affected by severe OSAS belonging to the late postmenopause group. After adjustment for potential confounding factors, associated factors for OSAS, regardless of its severity, were waist circumference, modified Mallampati score IV, and both postmenopause stages. For moderate to severe OSAS and severe OSAS, we found waist circumference and both postmenopause stages to be the main factors. We carried out a receiver operating characteristic curve analysis, which demonstrated that the cutoff value for waist circumference was 87.5 cm, with a maximum of 75.7% accuracy for the classification of women as OSAS or non-OSAS. **CONCLUSIONS:** OSAS is prevalent in postmenopausal women, especially in late postmenopause. This study highlights the association between waist circumference, early postmenopause and late postmenopause, and severity of OSAS. Our findings suggest that postmenopause stages may potentially exacerbate the presence of sleep disturbance and that reducing waist circumference may be an important strategy for managing OSAS in women.

Bone Miner Res. 2015 Feb 7. doi: 10.1002/jbmr.2478. [Epub ahead of print]

Life Expectancy in Patients Treated for Osteoporosis: Observational Cohort Study Using National Danish Prescription Data.

Abrahamsen B, Osmond C, Cooper C.

Osteoporosis is a chronic disease, carrying an elevated risk of fractures, morbidity and death. Long term treatment may be required but the long term risks with osteoporosis drugs remain incompletely understood. The competing risk of death may be a barrier to treating the oldest, yet this may not be rational if the risk of death is reduced by treatment. It is difficult to devise goal directed long term strategies for managing osteoporosis without firm information about residual lifetime expectancy in treated patients. We conducted an observational study in Danish national registries tracking prescriptions for osteoporosis drugs, comorbid conditions and deaths. We included 58,637 patients and 225,084 age- and gender matched control subjects. Information on deaths until the end of 2013 was retrieved, providing a follow-up period of 10-17 years. In men below age 80 and women below age 60, the relative risk of dying declined from being strongly increased in the first year to a stable but elevated level in subsequent years. In women older than 65-70 years of age there was only a small elevation in risk in the first year of treatment followed by lower than background mortality. The residual life expectancy of a 50-year old man beginning osteoporosis treatment was estimated to be 18.2 years and 7.5 years in a 75-year old man. Estimates in women were 26.4 years and 13.5 years. This study shows an excess mortality in men and in women below age 70 who are treated for osteoporosis, compared with the background population. This excess risk is more pronounced in the first few years on treatment. The average life expectancy of osteoporosis patients is in excess of fifteen years in women below the age of 75 and in men below the age of 60, highlighting the importance of developing tools for long term management.

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Hormone therapy might be underutilized in women with early menopause.

Lindh-Åstrand L, Hoffmann M, Järnstrått L, Fredriksson M, Hammar M, Spetz Holm AC.

STUDY QUESTION: Are Swedish women age 40-44 years with assumed early menopause 'undertreated' by hormone therapy (HT)? **SUMMARY ANSWER:** Many women with probable early menopause discontinue their HT after a short period of time. Thus, they fail to complete the recommended replacement up to age 51-52 years, the average age of menopause. **WHAT IS KNOWN ALREADY:** Spontaneous early menopause occurs in ~5% of women age 40-45 years. Regardless of the cause, women who experience hormonal menopause due to bilateral oophorectomy before the median age of spontaneous menopause are at increased risk of cardiovascular disease, neurological disease, osteoporosis, psychiatric illness and even death. **STUDY DESIGN, SIZE, and DURATION:** The study is descriptive, and epidemiological and was based on the use of national registers of dispensed drug prescriptions (HT) linking registers from the National Board of Health and Welfare and Statistics Sweden from 1 July 2005 until 31 December 2011. **PARTICIPANTS/MATERIALS, SETTING, METHODS:** The study population consisted of 310 404 women, 40-44 years old on 31 December 2005 who were followed from 1 July 2005 until 31

December 2011. MAIN RESULTS AND THE ROLE OF CHANCE: Only 0.9% of women 40-44 years old started HT during the study period. A majority of these women used HT <1 year. LIMITATIONS, REASONS FOR CAUTION: We do not know the indications that led to the prescription of HT but assume that early onset of menopause was the main reason. Because of the study design-making a retrospective study of registers-we can only speculate on the reasons for most of the women in this group discontinuing HT. Another limitation of this study is that we have a rather short observation time. However, we have up to now only been able to collect and combine the data since July 2005. WIDER IMPLICATIONS OF THE FINDINGS: As the occurrence of spontaneous early menopause in women age 40-45 is reported to be ~5%, the fact that <1% of Swedish women age 40-44 are prescribed HT, and can be shown also to have had the medication dispensed at a pharmacy suggests an unexpectedly low treatment rate. Some women with early menopause may have used combined contraceptives as supplementation therapy, but in Sweden HT is the recommended treatment for early menopause so any such women are not following this recommendation. Women who experience early menopause are at increased risk for overall morbidity and mortality, and can expect to benefit from HT until they have reached at least the median age of spontaneous menopause. It is therefore important to individualize the information given these women and to convey new knowledge in this area to gynaecologists and physicians in general as well as the recommendation that women in this group continue HT at least until the average age for spontaneous menopause is reached.