A SOCIEDADE PORTUGUESA DE ATEROSCLEROSE contou com a colaboração da SANOFI para o desenvolvimento deste projecto

SERUIÇO DE

A informação ao serviço da saúde

Dos Factores de Risco à Reabilitação das Doenças Vasculares 2017 - nº 3

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BMJ. 2017 Sep 22;358:j3984. doi: 10.1136/bmj.j3984.

Trends for prevalence and incidence of resistant hypertension: population based cohort study in the UK 1995-2015.

Sinnott SJ, Smeeth L, Williamson E, Douglas IJ.

Objective : To estimate the incidence and prevalence of resistant hypertension among a UK population treated for hypertension from 1995 to 2015. Design Cohort study. Setting Electronic health records from the UK Clinical Practice Research Datalink in primary care. Participants 1317290 users of antihypertensive drugs with a diagnosis of hypertension.

Main outcome measures Resistant hypertension was defined as concurrent use of three antihypertensive drugs inclusive of a diuretic, uncontrolled hypertension (≥140/90 mm Hg), and adherence to the prescribed drug regimen, or concurrent use of four antihypertensive drugs inclusive of a diuretic and adherence to the prescribed drug regimen. To determine incidence, the numerator was new cases of resistant hypertension and the denominator was person years of those with treated hypertension and at risk of developing resistant hypertension. To determine prevalence, the numerator was total number of cases with resistant hypertension and the denominator was those with treated hypertension. Prevalence and incidence were age standardised to the 2015 hypertensive population.

Results The age standardised incidence of resistant hypertension increased from 0.93 cases per 100 person years (95% confidence interval 0.87 to 1.00) in 1996 to a peak level of 2.07 cases per 100 person years (2.03 to 2.12) in 2004. Incidence then decreased to 0.42 cases per 100 person years (0.40 to 0.44) in 2015. Age standardised prevalence increased from 1.75% (95% confidence interval 1.66% to 1.83%) in 1995 to a peak of 7.76% (7.70% to 7.83%) in 2007. Prevalence then plateaued and subsequently declined to 6.46% (6.38% to 6.54%) in 2015. Compared with patients aged 65-69 years, those aged 80 or more years were more likely to have prevalent resistant hypertension throughout the study period.

Conclusions Prevalent resistant hypertension has plateaued and decreased in recent years, consistent with a decrease in incidence from 2004 onwards. Despite this, resistant hypertension is common in the UK hypertensive population. Given the importance of hypertension as a modifiable risk factor for cardiovascular disease, reducing uncontrolled hypertension should remain a population health focus.

PMID: 28939590 [Indexed for MEDLINE]

Am J Med Sci. 2017 Sep;354(3):240-245.

Awareness of Individual Cardiovascular Risk Factors and Self-Perception of Cardiovascular Risk in Women.

Monsuez JJ, Pham T, Karam N, Amar L, Chicheportiche-Ayache C, Menasché P, Desnos M, Dardel P, Weill I.

BACKGROUND: Cardiovascular risk factors (CVRFs) self-perception by women may be inaccurate. MATERIALS AND METHODS: A questionnaire was completed anonymously Online by women who self-reported their personal CVRF levels including age, weight, contraceptive use, menopausal status, smoking, diet and physical activities. Self-perceived risk was matched to actual cardiovascular risk according to the Framingham score.

RESULTS: Among 5,240 young and middle-aged women with a high educational level, knowledge of personal CVRFs increased with age, from 51-90% for blood pressure (BP), 22-45% for blood glucose and 15-47% for blood cholesterol levels, between 30 and 65 years, respectively. This knowledge was lower for smoking compared with nonsmoking women: 62.5% vs. 74.5% for BP (P < 0.001), 22.7% vs. 33.8% for blood glucose (P < 0.001), 21.9% vs. 32.0% for cholesterol levels (P < 0.001). Knowledge of BP level was reduced among women using an estrogen-progestogen contraception (56.8% vs. 62.1%, P = 0.0031) and even more reduced among smokers (52.2%, P < 0.001). Conversely, women with leisure-time physical or sportive activity (60.5%), were less overweight or obese (22.4% vs. 34.2%, P < 0.001). They reported better knowledge of BP (72.4% vs. 68.3%, P < 0.001), blood cholesterol (31.1% vs. 26.4%, P < 0.001) and glucose levels (32.7% vs. 27.8%, P < 0.001). Self-perceived cardiovascular risk was rated low by 1,279 (20.4%), moderate by 3,710 (63.3%) and high by 893 (16.3%) women. Among 3,386 women tested using the Framingham score, 40.8% were at low, 25.2% at moderate and 33.8% at high risk.

CONCLUSIONS: Knowledge of CVRFs and self-perception of individual risk are inaccurate in women. Educational interventions should be emphasized.

PMID: 28918829 [Indexed for MEDLINE]

MMWR Surveill Summ. 2017 Sep 15;66(16):1-144.

Surveillance for Certain Health Behaviors and Conditions Among States and Selected Local Areas - Behavioral Risk Factor Surveillance System, United States, 2013 and 2014.

Gamble S, Mawokomatanda T, Xu F, Chowdhury PP, Pierannunzi C, Flegel D, Garvin W, Town M.

PROBLEM: Chronic diseases and conditions (e.g., heart diseases, stroke, arthritis, and diabetes) are the leading causes of morbidity and mortality in the United States. These conditions are costly to the U.S. economy, yet they are often preventable or controllable. Behavioral risk factors (e.g., excessive alcohol consumption, tobacco use, poor diet, frequent mental distress, and insufficient sleep) are linked to the leading causes of morbidity and mortality. Adopting positive health behaviors (e.g., staying physically active, quitting tobacco use, obtaining routine physical checkups, and checking blood pressure and cholesterol levels) can reduce morbidity and mortality from chronic diseases and conditions. Monitoring the health risk behaviors, chronic diseases and conditions, access to health care, and use of preventive health services at multilevel public health points (states, territories, and metropolitan and micropolitan statistical areas [MMSA]) can provide important information for development and evaluation of health intervention programs.

REPORTING PERIOD: 2013 and 2014.

DESCRIPTION OF THE SYSTEM: The Behavioral Risk Factor Surveillance System (BRFSS) is an ongoing, state-based, random-digit-dialed telephone survey of noninstitutionalized adults aged ≥18 years residing in the United States. BRFSS collects data on health risk behaviors, chronic diseases and conditions, access to health care, and use of preventive health services and practices related to the leading causes of death and disability in the United States and participating territories. This is the first BRFSS report to include age-adjusted prevalence estimates. For 2013 and 2014, these age-adjusted prevalence estimates are presented for all 50 states, the District of Columbia, the Commonwealth of Puerto Rico, Guam, and selected MMSA.

RESULTS: Age-adjusted prevalence estimates of health status indicators, health care access and preventive practices, health risk behaviors, chronic diseases and conditions, and cardiovascular conditions vary by state, territory, and MMSA. Each set of proportions presented refers to the range of age-adjusted prevalence estimates of selected BRFSS measures as reported by survey respondents. The following are estimates for 2013. Adults reporting frequent mental distress: 7.7%-15.2% in states and territories and 6.3%-19.4% in MMSA. Adults with inadequate sleep: 27.6%-49.2% in states and territories and 26.5%-44.4% in MMSA. Adults aged 18-64 years having health care coverage: 66.9%-92.4% in states and territories and 60.5%-97.6% in MMSA. Adults identifying as current cigarette smokers: 10.1%-28.8% in states and territories and 6.1%-33.6% in MMSA. Adults reporting binge drinking during the past month: 10.5%-25.2% in states and territories and 7.2%-25.3% in MMSA. Adults with obesity: 21.0%-35.2% in states and territories and 12.1%-37.1% in MMSA. Adults aged ≥45 years with some form of arthritis: 30.6%-51.0% in states and territories and 27.6%-52.4% in

MMSA. Adults aged ≥45 years who have had coronary heart disease: 7.4%-17.5% in states and territories and 6.2%-20.9% in MMSA. Adults aged ≥45 years who have had a stroke: 3.1%-7.5% in states and territories and 2.3%-9.4% in MMSA. Adults with high blood pressure: 25.2%-40.1% in states and territories and 22.2%-42.2% in MMSA. Adults with high blood cholesterol: 28.8%-38.4% in states and territories and 26.3%-39.6% in MMSA. The following are estimates for 2014. Adults reporting frequent physical distress: 7.8%-16.0% in states and territories and 6.2%-18.5% in MMSA. Women aged 21-65 years who had a Papanicolaou test during the past 3 years: 67.7%-87.8% in states and territories and 68.0%-94.3% in MMSA. Adults aged 50-75 years who received colorectal cancer screening on the basis of the 2008 U.S. Preventive Services Task Force recommendation: 42.8%-76.7% in states and territories and 49.1%-79.6% in MMSA. Adults with inadequate sleep: 28.4%-48.6% in states and territories and 25.4%-45.3% in MMSA. Adults reporting binge drinking during the past month: 10.7%-25.1% in states and territories and 6.7%-26.3% in MMSA. Adults aged ≥45 years who have had coronary heart disease: 8.0%-17.1% in states and territories and 7.6%-19.2% in MMSA. Adults aged ≥45 years with some form of arthritis: 31.2%-54.7% in states and territories and 28.4%-54.7% in MMSA. Adults with obesity: 21.0%-35.9% in states and territories and 19.7%-42.5% in MMSA.

INTERPRETATION: Prevalence of certain chronic diseases and conditions, health risk behaviors, and use of preventive health services varies among states, territories, and MMSA. The findings of this report highlight the need for continued monitoring of health status, health care access, health behaviors, and chronic diseases and conditions at state and local levels.

PUBLIC HEALTH ACTION: State and local health departments and agencies can continue to use BRFSS data to identify populations at risk for certain unhealthy behaviors and chronic diseases and conditions. Data also can be used to design, monitor, and evaluate public health programs at state and local levels.

PMID: 28910267 [Indexed for MEDLINE]

Am Heart J. 2017 Sep;191:82-90.

Blood pressure reactivity to psychological stress is associated with clinical outcomes in patients with heart failure.

Sherwood A, Hill LK, Blumenthal JA, Adams KF Jr, Paine NJ, Koch GG, O'Connor CM, Johnson KS, Hinderliter AL.

INTRODUCTION: Cardiovascular (CV) reactivity to psychological stress has been implicated in the development and exacerbation of cardiovascular disease (CVD). Although high CV reactivity traditionally is thought to convey greater risk of CVD, the relationship between reactivity and clinical outcomes is inconsistent and may depend on the patient population under investigation. The present study examined CV reactivity in patients with heart failure (HF) and its potential association with long-term clinical outcomes.

METHODS: One hundred ninety-nine outpatients diagnosed with HF, with ejection fraction \leq 40%, underwent an evaluation of blood pressure (BP) and heart rate reactivity to a laboratory-based simulated public-speaking stressor. Cox proportional hazards regression models were used to examine the prospective association between BP and heart rate reactivity on a combined end point of death or CV hospitalization over a 5-year median follow-up period.

RESULTS: Both systolic blood pressure (SBP) and diastolic blood pressure (DBP) reactivity, quantified as continuous variables, were inversely related to risk of death or CV hospitalization (Ps < .01) after controlling for established risk factors, including HF disease severity and etiology. In similar models, heart rate reactivity was unrelated to outcome (P = .12). In models with tertiles of reactivity, high SBP reactivity, compared with intermediate SBP reactivity, was associated with lower risk (hazard ratio [HR] = .498, 95% CI .335-.742, P =.001), whereas low SBP reactivity did not differ from intermediate reactivity. For DBP, high reactivity was marginally associated with lower risk compared with intermediate DBP reactivity (HR = .767, 95% CI .515-1.14, P =.193), whereas low DBP reactivity was associated with greater risk (HR = 1.49, 95% CI 1.027-2.155, P =.0359). No relationship of heart rate reactivity to outcome was identified.

CONCLUSIONS: For HF patients with reduced ejection fraction, a robust increase in BP evoked by a laboratory-based psychological challenge was associated with lower risk for adverse CVD events and may be a novel and unique marker of left ventricular systolic reserve that is accompanied by a more favorable long-term prognosis.

PMID: 28888274 [Indexed for MEDLINE]

Trends in the Prevalence, Awareness, Treatment, and Control of Hypertension Among Young Adults in the United States, 1999 to 2014.

Zhang Y, Moran AE.

Overall hypertension prevalence has not changed in the United States in recent decades although awareness, treatment, and control improved. However, hypertension epidemiology and its temporal trends may differ in younger adults compared with older adults. Our study included 41 331 participants ≥18 years of age from 8 National Health and Nutrition Examination Surveys (1999-2014) and estimated temporal trends of hypertension, awareness, treatment, and control among young adults (age, 18-39 years) compared with middle-age (age, 40-59 years) and older adults (age, ≥60 years). In 2013 to 2014, 7.3% of the US young adults had hypertension. During 1999 to 2014, young adults saw larger increases in hypertension awareness, treatment, and control than did older adults. However, all of these components of hypertension control were lower among young adults compared with middleaged or older adults (74.7% younger versus 81.9% middle versus 88.4% older for awareness; 50.0% versus 70.3% versus 83.0% for treatment; and 40.2% versus 56.7% versus 54.4% for control). Worse hypertension awareness, treatment, and control in young adults overall were mostly driven by worse measures in young adult men compared with young adult women. More frequent healthcare visits by young adult women explained ≈28% of the sex-related difference in awareness, 60% of the difference in treatment, and 52% of the difference in control. These findings suggest that improved access to and engagement in medical care might improve hypertension control in young adults, particularly young adult men, and reduce life-time cardiovascular risk.

PMID: 28847890 [Indexed for MEDLINE]

JAMA. 2017 Sep 12;318(10):947-956.

Association of Genetic Variants Related to CETP Inhibitors and Statins With Lipoprotein Levels and Cardiovascular Risk.

Ference BA, Kastelein JJP, Ginsberg HN, Chapman MJ, Nicholls SJ, Ray KK, Packard CJ, Laufs U, Brook RD), Oliver-Williams C, Butterworth AS, Danesh J, Smith GD, Catapano AL, Sabatine MS.

Importance: Some cholesteryl ester transfer protein (CETP) inhibitors lower low-density lipoprotein cholesterol (LDL-C) levels without reducing cardiovascular events, suggesting that the clinical benefit of lowering LDL-C may depend on how LDL-C is lowered.

Objective: To estimate the association between changes in levels of LDL-C (and other lipoproteins) and the risk of cardiovascular events related to variants in the CETP gene, both alone and in combination with variants in the 3-hydroxy-3-methylglutaryl-CoA reductase (HMGCR) gene.

Design, Setting, and Participants: Mendelian randomization analyses evaluating the association between CETP and HMGCR scores, changes in lipid and lipoprotein levels, and the risk of cardiovascular events involving 102 837 participants from 14 cohort or case-control studies conducted in North America or the United Kingdom between 1948 and 2012. The associations with cardiovascular events were externally validated in 189 539 participants from 48 studies conducted between 2011 and 2015.

Exposures: Differences in mean high-density lipoprotein cholesterol (HDL-C), LDL-C, and apolipoprotein B (apoB) levels in participants with CETP scores at or above vs below the median. Main Outcomes and Measures: Odds ratio (OR) for major cardiovascular events. Results: The primary analysis included 102 837 participants (mean age, 59.9 years; 58% women) who experienced 13 821 major cardiovascular events. The validation analyses included 189 539 participants (mean age, 58.5 years; 39% women) with 62 240 cases of coronary heart disease (CHD). Considered alone, the CETP score was associated with higher levels of HDL-C, lower LDL-C, concordantly lower apoB, and a corresponding lower risk of major vascular events (OR, 0.946 [95% CI, 0.921-0.972]) that was similar in magnitude to the association between the HMGCR score and risk of major cardiovascular events per unit change in levels of LDL-C (and apoB). When combined with the HMGCR score, the CETP score was associated with the same reduction in LDL-C levels but an attenuated reduction in apoB levels and a corresponding attenuated nonsignificant risk of major cardiovascular events (OR, 0.985 [95% CI, 0.955-1.015]). In external validation analyses, a genetic score consisting of variants with naturally occurring discordance between levels of LDL-C and apoB was associated with a similar risk

of CHD per unit change in apoB level (OR, 0.782 [95% CI, 0.720-0.845] vs 0.793 [95% CI, 0.774-0.812]; P=.79 for difference), but a significantly attenuated risk of CHD per unit change in LDL-C level (OR, 0.916 [95% CI, 0.890-0.943] vs 0.831 [95% CI, 0.816-0.847]; P<.001) compared with a genetic score associated with concordant changes in levels of LDL-C and apoB.

Conclusions and Relevance: Combined exposure to variants in the genes that encode the targets of CETP inhibitors and statins was associated with discordant reductions in LDL-C and apoB levels and

a corresponding risk of cardiovascular events that was proportional to the attenuated reduction in apoB but significantly less than expected per unit change in LDL-C. The clinical benefit of lowering LDL-C levels may therefore depend on the corresponding reduction in apoB-containing lipoprotein particles.

PMID: 28846118 [Indexed for MEDLINE]

Prevalence of type 2 diabetes and impaired fasting glucose in patients affected by rheumatoid arthritis: Results from a cross-sectional study.

Ruscitti P, Ursini F, Cipriani P, Ciccia F, Liakouli V, Carubbi F, Guggino G, Berardicurti O, Grembiale R, Triolo G, De Sarro G, Giacomelli R.

Although the better management of rheumatoid arthritis (RA) has significantly improved the long-term outcome of affected patients, a significant proportion of these may develop associated comorbidities including cardiometabolic complications. However, it must be pointed out that a comprehensive cardiometabolic evaluation is still poorly integrated into the management of RA patients, due to a limited awareness of the problem, a lack of appropriate clinical studies, and optimal strategies for cardiovascular (CV) risk reduction in RA. In addition, although several studies investigated the possible association between traditional CV risk factors and RA, conflicting results are still available. On this basis, we planned this cross-sectional study, aimed at investigating the prevalence of type 2 diabetes (T2D) and impaired fasting glucose (IFG) in RA patients compared with age- and gendermatched control individuals. Furthermore, we analyzed the role of both traditional and RA-related CV risk factors in predicting T2D and IFG. We observed an increased prevalence of T2D in RA patients when compared with age- and gender-matched controls. Regression analyses demonstrated that the presence of high blood pressure (HBP), a longer disease duration, and exposure to corticosteroids (CCS) were significantly associated with an increased likelihood of being classified as T2D. In addition, we observed an increased prevalence of IFG in RA patients when compared with age- and gender-matched controls. Regression analyses demonstrated that a higher body mass index (BMI), the presence of metabolic syndrome (MetS), higher levels of total cholesterol, the presence of radiographic damage, and higher serum levels of C-reactive protein (CRP) were significantly associated with an increased likelihood of presenting IFG. In this cross-sectional study, we observed an increased prevalence of T2D and IFG in an Italian cohort of RA patients when compared with ageand gender-matched control individuals. Interestingly, both RA-specific features, such as disease duration, CCS exposure, and radiographic damage, and traditional CV risk factors, such as HBP and MetS, were significantly associated with glucose metabolism abnormalities.

PMCID: PMC5572029

PMID: 28834907 [Indexed for MEDLINE]

Hypertension. 2017 Oct;70(4):721-728.

Increased Risk of New-Onset Hypertension After Shock Wave Lithotripsy in Urolithiasis: A Nationwide Cohort Study.

Huang SW, Tsai CY, Wang J, Pu YS, Chen PC, Huang CY, Chien KL.

Although shock wave lithotripsy is minimally invasive, earlier studies argued that it may increase patients' subsequent risk of hypertension and diabetes mellitus. This study evaluated the association between shock wave lithotripsy and new-onset hypertension or diabetes mellitus. The Taiwanese National Health Insurance Research Database was used to identify 20 219 patients aged 18 to 65 years who underwent the first stone surgical treatment (shock wave lithotripsy or ureterorenoscopic lithotripsy) between January 1999 and December 2011. A Cox proportional model was applied to evaluate associations. Time-varying Cox models were applied to evaluate the association between the number of shock wave lithotripsy sessions and the incidence of hypertension or diabetes mellitus. After a median follow-up of 74.9 and 82.6 months, 2028 and 688 patients developed hypertension in the shock wave lithotripsy and ureterorenoscopic lithotripsy groups, respectively. Patients who underwent shock wave lithotripsy had a higher probability of developing hypertension than patients who underwent ureterorenoscopic lithotripsy, with a hazard ratio of 1.20 (95% confidence interval, 1.10-1.31) after adjusting for covariates. The risk increased as the number of shock wave lithotripsy sessions increased. However, the diabetes mellitus risk was similar in the shock wave lithotripsy and ureterorenoscopic lithotripsy groups. Furthermore, the hazard ratio did not increase as the number of shock wave lithotripsy sessions increased. Shock wave lithotripsy consistently increased the incidence of hypertension on long-term follow-up. Therefore, alternatives to urolithiasis treatment (eg, endoscopic surgery or medical expulsion therapy) could avoid the hypertension risk. Furthermore, avoiding multiple sessions of shock wave lithotripsy could also evade the hypertension risk.

PMID: 28827478 [Indexed for MEDLINE]

Pediatrics. 2017 Sep;140(3). pii: e20170338.

Sleep Duration and Risk of Type 2 Diabetes.

Rudnicka AR, Nightingale CM, Donin AS, Sattar N, Cook DG, Whincup PH, Owen CG.

BACKGROUND: Associations between sleep duration and type 2 diabetes (T2D) risk markers in childhood have been little studied. We examined associations between self-reported sleep duration and T2D risk markers in children.

METHODS: Cross-sectional study of 4525 multiethnic UK children aged 9 to 10 years. Sleep time was calculated from self-reported usual time of going to bed and getting up on a school day, validated in a subset using accelerometers. Fasting blood samples provided levels of serum lipids and insulin, plasma glucose, and HbA1c. Physical measures included height, weight, bioimpedance, and blood pressure. Multilevel linear regression models of anthropometric, T2D, and cardiovascular risk markers with sleep duration were adjusted for sex, age, month, ethnicity, socioeconomic position, observer (physical measures only), and random effect of school.

RESULTS: On average, children slept 10.5 hours per night (95% range 8.0-12.0 hours). There were strong inverse graded relationships between sleep duration, adiposity, and diabetes risk markers. In adjusted models, a 1-hour-longer sleep duration was associated with 0.19 lower BMI (95% confidence interval [CI] 0.09 to 0.28), 0.03 kg/m(5) lower fat mass index (95% CI 0.00 to 0.05 kg/m(5)), 2.9% lower homeostasis model assessment insulin resistance (95% CI 1.2% to 4.4%), and 0.24% lower fasting glucose (95% CI 0.03% to 0.44%); there was no association with HbA1c or cardiovascular risk. Associations with insulin and glucose remained after an additional adjustment for adiposity markers. CONCLUSIONS: The finding of an inverse association between sleep duration and T2D risk markers

in childhood is novel. Intervention studies are needed to establish the causality of these associations, which could provide a simple strategy for early T2D prevention.

PMID: 28811317 [Indexed for MEDLINE]

J Am Coll Cardiol. 2017 Aug 15;70(7):883-893.

Primary Prevention of Cardiovascular Disease in Diabetes Mellitus.

Newman JD, Schwartzbard AZ, Weintraub HS, Goldberg IJ, Berger JS.

Type 2 diabetes mellitus (T2D) is a major risk factor for cardiovascular disease (CVD), the most common cause of death in T2D. Yet, <50% of U.S. adults with T2D meet recommended guidelines for CVD prevention. The burden of T2D is increasing: by 2050, approximately 1 in 3 U.S. individuals may have T2D, and patients with T2D will comprise an increasingly large proportion of the CVD population. The authors believe it is imperative that we expand the use of therapies proven to reduce CVD risk in patients with T2D. The authors summarize evidence and guidelines for lifestyle (exercise, nutrition, and weight management) and CVD risk factor (blood pressure, cholesterol and blood lipids, glycemic control, and the use of aspirin) management for the prevention of CVD among patients with T2D. The authors believe appropriate lifestyle and CVD risk factor management has the potential to significantly reduce the burden of CVD among patients with T2D.

PMID: 28797359 [Indexed for MEDLINE]

Presse Med. 2017 Jul - Aug; 46(7-8 Pt 1):697-702.

[Smoking and blood pressure: A complex relationship].

[Article in French]

Madika AL, Mounier-Vehier C.

Hypertension and tobacco smoking are two major modifiable risk factors for atheromatous disease and its cardiovascular complications. If systolic hypertension (SBP≥140mmHg and DBP<90mmHg) is the leading risk factor for stroke, smoking (nicotine) has a more powerful impact on coronary events, aortic aneurysms, and peripheral artery disease. Smoking can transiently modify the regulation of blood pressure (BP) by a swift effect on the autonomic nervous system. It also accelerates arterial aging, which plays a role in chronic hypertension. Chronic sympathetic activation induced by tobacco smoking also has some involvement in lipid metabolism and insulin resistance, both implicated in atheromatous disease. Thus, smoking can contribute to the development of atheromatous renal artery stenosis, which is an aggravating cause of hypertension. It may also reduce the effectiveness of most antihypertensive drugs. Finally, it is often associated with increased alcohol consumption. All these factors may contribute to poor blood pressure control in these high-risk CV patients. Smoking cessation is effective regardless of patient age and length of consumption. Every effort should thus be made to support smoking cessation. This is the objective of the French "Plan Sans Tabac" (No Tobacco Plan) and the related actions conducted by the French Federation of Cardiology.

PMID: 28760595 [Indexed for MEDLINE]

Presse Med. 2017 Jul - Aug;46(7-8 Pt 1):708-713.

[The gut microbiota, a new cardiovascular risk factor?]

[Article in French]

Chong-Nguyen C, Duboc H, Sokol H.

The gut microbiota is considered as our other "brain" and is implicated in several regulation of physiological metabolisms. The circulating level of TMAO, a metabolite of the gut microbiota, is directly correlated to the occurrence of cardiovascular events. Bile acids are protective metabolites against cardiovascular diseases through their anti-inflammatory and anti-atherogenic effects. The disturbance in the metabolism and the composition of the gut microbiota is called "dysbiosis". Understanding the implication of the gut microbiota and developing new therapeutic strategies are promising research fields to manage metabolic and cardiovascular diseases.

PMID: 28756077 [Indexed for MEDLINE]

PLoS One. 2017 Jul 19;12(7):e0179508.

Association between urinary biomarkers of total sugars intake and measures of obesity in a cross-sectional study.

Campbell R, Tasevska N, Jackson KG, Sagi-Kiss V, di Paolo N, Mindell JS, Lister SJ, Khaw KT, Kuhnle GGC.

Obesity is an important modifiable risk factor for chronic diseases. While there is increasing focus on the role of dietary sugars, there remains a paucity of data establishing the association between sugar intake and obesity in the general public. The objective of this study was to investigate associations of estimated sugar intake with odds for obesity in a representative sample of English adults. We used data from 434 participants of the 2005 Health Survey of England. Biomarkers for total sugar intake were measured in 24 h urine samples and used to estimate intake. Linear and logistic regression analyses were used to investigate associations between biomarker-based estimated intake and measures of obesity (body mass intake (BMI), waist circumference and waist-to-hip ratio) and obesity risk, respectively. Estimated sugar intake was significantly associated with BMI, waist circumference and waist-to-hip ratio; these associations remained significant after adjustment for estimated protein intake as a marker of non-sugar energy intake. Estimated sugar intake was also associated with increased odds for obesity based on BMI (OR 1.02; 95%CI 1.00-1.04 per 10g), waist-circumference (1.03; 1.01-1.05) and waist-to-hip ratio (1.04; 1.02-1.06); all OR estimates remained significant after adjusting for estimated protein intake. Our results strongly support positive associations between total sugar intake, measures of obesity and likelihood of being obese. It is the first time that such an association has been shown in a nationally-representative sample of the general population using a validated biomarker. This biomarker could be used to monitor the efficacy of public health interventions to reduce sugar intake.

PMCID: PMC5517003 PMID: 28723954 [Indexed for MEDLINE] Int Heart J. 2017 Aug 3;58(4):475-480.

Coronary Artery Disease and Type 2 Diabetes Mellitus.

Naito R, Miyauchi K.

Type 2 diabetes mellitus (T2DM) is a major risk factor of coronary artery diseases (CAD). Clinical outcomes in CAD with T2DM are poor despite improvement in medications and intervention devices. Coronary artery bypass grafting (CABG) is superior to percutaneous coronary intervention (PCI) in treating diabetic patients with multivessel coronary artery diseases (MVD). However, selecting a revascularization strategy should depend not only on the lesion complexity but also on the patient's background and comorbidities. In addition, comprehensive risk management with medical and non-pharmacological therapies is important, as is confirmation of whether risk managements are appropriately achieved. Recently, novel anti-diabetic drugs have been demonstrated to have effectiveness in reducing cardiovascular events, which was independent of their glucose-lowering effect. Furthermore, non-pharmacological interventions using exercise and diet during the earlier stages of abnormal glucose metabolism might be beneficial in preventing the development or progression of T2DM and reducing the incidence of cardiovascular events.

PMID: 28717115 [Indexed for MEDLINE]

JAMA Intern Med. 2017 Sep 1;177(9):1354-1360.

Application of a Lifestyle-Based Tool to Estimate Premature Cardiovascular Disease Events in Young Adults: The Coronary Artery Risk Development in Young Adults (CARDIA) Study.

Gooding HC, Ning H, Gillman MW, Shay C, Allen N, Goff DC Jr, Lloyd-Jones D, Chiuve S.

Importance: Few tools exist for assessing the risk for early atherosclerotic cardiovascular disease (ASCVD) events in young adults. Objective: To assess the performance of the Healthy Heart Score (HHS), a lifestyle-based tool that estimates ASCVD events in older adults, for ASCVD events occurring before 55 years of age.

Design, Setting, and Participants: This prospective cohort study included 4893 US adults aged 18 to 30 years from the Coronary Artery Risk Development in Young Adults (CARDIA) study. Participants underwent measurement of lifestyle factors from March 25, 1985, through June 7, 1986, and were followed up for a median of 27.1 years (interquartile range, 26.9-27.2 years). Data for this study were analyzed from February 24 through December 12, 2016.

Exposures: The HHS includes age, smoking status, body mass index, alcohol intake, exercise, and a diet score composed of self-reported daily intake of cereal fiber, fruits and/or vegetables, nuts, sugarsweetened beverages, and red and/or processed meats. The HHS in the CARDIA study was calculated using sex-specific equations produced by its derivation cohorts.

Main Outcomes and Measures: The ability of the HHS to assess the 25-year risk for ASCVD (death from coronary heart disease, nonfatal myocardial infarction, and fatal or nonfatal ischemic stroke) in the total sample, in race- and sex-specific subgroups, and in those with and without clinical ASCVD risk factors at baseline. Model discrimination was assessed with the Harrell C statistic; model calibration, with Greenwood-Nam-D'Agostino statistics.

Results: The study population of 4893 participants included 2205 men (45.1%) and 2688 women (54.9%) with a mean (SD) age at baseline of 24.8 (3.6) years; 2483 (50.7%) were black; and 427 (8.7%) had at least 1 clinical ASCVD risk factor (hypertension, hyperlipidemia, or diabetes types 1 and 2). Among these participants, 64 premature ASCVD events occurred in women and 99 in men. The HHS showed moderate discrimination for ASCVD risk assessment in this diverse population of mostly healthy young adults (C statistic, 0.71; 95% CI, 0.66-0.76); it performed better in men (C statistic, 0.74; 95% CI, 0.68-0.79) than in women (C statistic, 0.69; 95% CI, 0.62-0.75); in white (C statistic, 0.77; 95% CI, 0.71-0.84) than in black (C statistic, 0.66; 95% CI, 0.60-0.72) participants; and in those without (C statistic, 0.71; 95% CI, 0.66-0.76) vs with (C statistic, 0.64; 95% CI, 0.55-0.73) clinical risk factors at baseline. The HHS was adequately calibrated overall and within each subgroup. Conclusions and Relevance: The HHS, when measured in younger persons without ASCVD risk factors, performs moderately well in assessing risk for ASCVD events by early middle age. Its reliance

on self-reported, modifiable lifestyle factors makes it an attractive tool for risk assessment and counseling for early ASCVD prevention.

Am J Cardiol. 2017 Sep 1;120(5):868-873.

Reliability of Cardiovascular Risk Calculators to Estimate Accurately the Risk of Cardiovascular Disease in Patients With Sarcoidosis.

Ungprasert P, Matteson EL, Crowson CS.

Chronic inflammation is an independent risk factor for cardiovascular disease (CVD), but most risk calculators, including the Framingham risk score (FRS) and the American College of Cardiology (ACC)/American Heart Association (AHA) risk score do not account for it. These calculators underestimate cardiovascular risk in patients with rheumatoid arthritis and systemic lupus erythematosus. To date, how these scores perform in the estimation of CVD risk in patients with sarcoidosis has not been assessed. In this study, the FRS and the ACC/AHA risk score were calculated for a previously identified cohort of patients with incident cases of sarcoidosis in Olmsted County, Minnesota, United States, from 1989 to 2013 as well as their gender- and age-matched comparators. The standardized incidence ratio (SIR) was estimated as the ratio of the predicted and observed numbers of CVD events. All CVD events were identified by diagnosis codes and were verified by individual medical record reviews. The predicted number of CVD events among 188 cases by FRS was 11.8 and the observed number of CVD events was 34, which corresponded to an SIR of 2.88 (95% confidence interval 2.06 to 4.04). FRS underestimated the risk of CVD events in patients with sarcoidosis by gender, age and severity of sarcoidosis. The predicted number of CVD events among cases by ACC/AHA risk score was 4.6 and the observed number of CVD events was 19, corresponding to an SIR of 4.11 (95% confidence interval 2.62 to 6.44). In conclusion, the FRS and the ACC/AHA risk score underestimate the risk of CVD in patients with sarcoidosis.

PMCID: PMC5564423 [Available on 2018-09-01] PMID: 28705378 [Indexed for MEDLINE]

Behavioral Counseling to Promote a Healthful Diet and Physical Activity for Cardiovascular Disease Prevention in Adults Without Cardiovascular Risk Factors: US Preventive Services Task Force Recommendation Statement.

US Preventive Services Task Force, Grossman DC, Bibbins-Domingo K, Curry SJ, Barry MJ, Davidson KW, Doubeni CA, Epling JW Jr, Kemper AR, Krist AH, Kurth AE, Landefeld CS, Mangione CM, Phipps MG, Silverstein M, Simon MA, Tseng CW.

Importance: Adults who adhere to national guidelines for a healthful diet and physical activity have lower rates of cardiovascular morbidity and mortality than those who do not. All persons, regardless of their risk status for cardiovascular disease (CVD), can gain health benefits from healthy eating behaviors and appropriate physical activity.

Objective: To update the 2012 US Preventive Services Task Force (USPSTF) recommendation on behavioral counseling to promote a healthful diet and physical activity for cardiovascular disease prevention among adults without obesity who do not have cardiovascular risk factors (hypertension, dyslipidemia, abnormal blood glucose levels, or diabetes).

Evidence Review: The USPSTF reviewed the evidence on whether primary care-relevant counseling interventions to promote a healthful diet, physical activity, or both improve health outcomes, intermediate outcomes associated with CVD, or dietary or physical activity behaviors in adults; interventions to reduce sedentary behaviors; and the harms of behavioral counseling interventions.

Findings: Counseling interventions result in improvements in healthful behaviors and small but potentially important improvements in intermediate outcomes, including reductions in blood pressure and low-density lipoprotein cholesterol levels and improvements in measures of adiposity. The overall magnitude of benefit related to these interventions is positive but small. The potential harms are at most small, leading the USPSTF to conclude that these interventions have a small net benefit for adults without obesity who do not have CVD risk factors.

Conclusions and Recommendation: The USPSTF recommends that primary care professionals individualize the decision to offer or refer adults without obesity who do not have hypertension, dyslipidemia, abnormal blood glucose levels, or diabetes to behavioral counseling to promote a healthful diet and physical activity. Existing evidence indicates a positive but small benefit of behavioral counseling for the prevention of CVD in this population. Persons who are interested and ready to make behavioral changes may be most likely to benefit from behavioral counseling. (C recommendation).

PMID: 28697260 [Indexed for MEDLINE]

JAMA. 2017 Jul 11;318(2):175-193.

Behavioral Counseling to Promote a Healthful Diet and Physical Activity for Cardiovascular Disease Prevention in Adults Without Known Cardiovascular Disease Risk Factors: Updated Evidence Report and Systematic Review for the US Preventive Services Task Force.

Patnode CD, Evans CV, Senger CA, Redmond N, Lin JS.

Importance: Unhealthful dietary patterns, low levels of physical activity, and high sedentary time increase the risk of cardiovascular disease.

Objective: To systematically review the evidence on the benefits and harms of behavioral counseling for the primary prevention of cardiovascular disease in adults without known cardiovascular risk factors to inform the US Preventive Services Task Force. Data Sources: MEDLINE, PubMed, Cochrane Central Register of Controlled Trials, and PsycINFO for studies published in the English language between January 1, 2013, and May 25, 2016, and ongoing surveillance in targeted publications through March 24, 2017. Studies included in the previous review were reevaluated for inclusion. Study Selection: Randomized clinical trials of behavioral interventions targeting improved diet, increased physical activity, decreased sedentary time, or a combination of these among adults without known hypertension, dyslipidemia, diabetes, or impaired fasting glucose.

Data Extraction and Synthesis: Independent critical appraisal and data abstraction by 2 reviewers.

Main Outcomes and Measures: Cardiometabolic health and intermediate outcomes, behavioral outcomes, and harms related to interventions.

Results: Eighty-eight studies (N=121 190) in 145 publications were included. There was no consistent benefit of the interventions on all-cause or cardiovascular mortality or morbidity (4 trials [n=51 356]) or health-related quality of life (10 trials [n=52 423]). There was evidence of small, statistically significant between-group mean differences for systolic blood pressure (-1.26 mm Hg [95% CI, -1.77 to -0.75]; 22 trials [n=57 953]), diastolic blood pressure (-0.49 mm Hg [95% CI, -0.82 to -0.16]; 23 trials [n=58 022]), low-density lipoprotein cholesterol level (-2.58 mg/dL [95% CI, -4.30 to -0.85]; 13 trials [n=5554]), total cholesterol level (-2.85 mg/dL [95% CI, -4.95 to -0.75]; 19 trials [n=9325]), and body mass index (-0.41 [95% CI, -0.62 to -0.19]; 20 trials [n=55 059]) at 6 to 12 months as well as small-to-modest associations with dietary and physical activity behaviors. There was no evidence of greater incidence of serious adverse events, injuries, or falls in intervention vs control participants.

Conclusions and Relevance: Diet and physical activity behavioral interventions for adults not at high risk for cardiovascular disease result in consistent modest benefits across a variety of important intermediate health outcomes across 6 to 12 months, including blood pressure, low-density lipoprotein and total cholesterol levels, and adiposity, with evidence of a dose-response effect, with higher-

intensity interventions conferring greater improvements. There is very limited evidence on longer-term intermediate and health outcomes or on harmful effects of these interventions.

PMID: 28697259 [Indexed for MEDLINE] Nutr Metab Cardiovasc Dis. 2017 Jul;27(7):651-656.

Is low iodine a risk factor for cardiovascular disease in Americans without thyroid dysfunction? Findings from NHANES.

Tran HV, Erskine NA, Kiefe CI, Barton BA, Lapane KL, Do VTH, Goldberg RJ.

BACKGROUND AND AIMS: Low body iodine levels are associated with cardiovascular disease, in part through alterations in thyroid function. While this association suggested from animal studies, it lacks supportive evidence in humans. This study examined the association between urine iodine levels and presence of coronary artery disease (CAD) and stroke in adults without thyroid dysfunction. METHODS AND RESULTS: This cross-sectional study included 2440 adults (representing a weighted n = 91,713,183) aged \geq 40 years without thyroid dysfunction in the nationally-representative 2007-2012 National Health and Nutrition Examination Survey. The age and sex-adjusted urine iodine/creatinine ratio (aICR) was categorized into low (aICR<116 μ g/day), medium (116 μ g/day ≤ aICR < 370 μ g/day), and high (alCR ≥ 370µg/day) based on lowest/highest quintiles. Stroke and CAD were from selfreported physician diagnoses. We examined the association between low urine aICR and CAD or stroke using multivariable logistic regression modeling. The mean age of this population was 56.0 years, 47% were women, and three quarters were non-Hispanic whites. Compared with high urine iodine levels, multivariable adjusted odds ratios aOR (95% confidence intervals) for CAD were statistically significant for low, aOR = 1.97 (1.08-3.59), but not medium, aOR = 1.26 (0.75-2.13) urine iodine levels. There was no association between stroke and low, aOR = 1.12 (0.52-2.44) or medium, aOR = 1.48 (0.88-2.48) urine iodine levels.

CONCLUSION: The association between low urine iodine levels and CAD should be confirmed in a prospective study with serial measures of urine iodine. If low iodine levels precede CAD, then this potential and modifiable new CAD risk factor might have therapeutic implications.

PMID: 28689680 [Indexed for MEDLINE]

J Am Coll Cardiol. 2017 Jul 11;70(2):230-251.

Oxidative Stress and Cardiovascular Risk: Obesity, Diabetes, Smoking, and Pollution: Part 3 of a 3-Part Series.

Niemann B, Rohrbach S, Miller MR, Newby DE, Fuster V, Kovacic JC.

Oxidative stress occurs whenever the release of reactive oxygen species (ROS) exceeds endogenous antioxidant capacity. In this paper, we review the specific role of several cardiovascular risk factors in promoting oxidative stress: diabetes, obesity, smoking, and excessive pollution. Specifically, the risk of developing heart failure is higher in patients with diabetes or obesity, even with optimal medical treatment, and the increased release of ROS from cardiac mitochondria and other sources likely contributes to the development of cardiac dysfunction in this setting. Here, we explore the role of different ROS sources arising in obesity and diabetes, and the effect of excessive ROS production on the development of cardiac lipotoxicity. In parallel, contaminants in the air that we breathe pose a significant threat to human health. This paper provides an overview of cigarette smoke and urban air pollution, considering how their composition and biological effects have detrimental effects on cardiovascular health.

PMCID: PMC5568826 [Available on 2018-07-11] PMID: 28683970 [Indexed for MEDLINE] Hypertension. 2017 Aug;70(2):435-443.

Blood Pressure and Risk of Cardiovascular Events in Patients on Chronic Hemodialysis: The CRIC Study (Chronic Renal Insufficiency Cohort).

Bansal N, McCulloch CE, Lin F, Alper A, Anderson AH, Cuevas M, Go AS, Kallem R, Kusek JW, Lora CM, Lustigova E, Ojo A, Rahman M, Robinson-Cohen C, Townsend RR, Wright J, Xie D, Hsu CY; CRIC Study Investigators*.

We recently reported a linear association between higher systolic blood pressure (SBP) and risk of mortality in hemodialysis patients when SBP is measured outside of the dialysis unit (out-of-dialysisunit-SBP), despite there being a U-shaped association between SBP measured at the dialysis unit (dialysis-unit-SBP) with risk of mortality. Here, we explored the relationship between SBP with cardiovascular events, which has important treatment implications but has not been well elucidated. Among 383 hemodialysis participants enrolled in the prospective CRIC study (Chronic Renal Insufficiency Cohort), multivariable splines and Cox models were used to study the association between SBP and adjudicated cardiovascular events (heart failure, myocardial infarction, ischemic stroke, and peripheral artery disease), controlling for differences in demographics, cardiovascular disease risk factors, and dialysis parameters. Dialysis-unit-SBP and out-of-dialysis-unit-SBP were modestly correlated (r=0.34; P<0.001). We noted a U-shaped association of dialysis-unit-SBP and risk of cardiovascular events, with the nadir risk between 140 and 170 mmHg. In contrast, there was a linear stepwise association between out-of-dialysis-unit-SBP with risk of cardiovascular events. Participants with out-of-dialysis-unit-SBP ≥128 mmHg (top 2 quartiles) had >2-fold increased risk of cardiovascular events compared with those with out-of-dialysis-unit-SBP ≤112 mmHg (3rd SBP quartile: adjusted hazard ratio, 2.08 [95% confidence interval, 1.12-3.87] and fourth SBP quartile: adjusted hazard ratio, 2.76 [95% confidence interval, 1.42-5.33]). In conclusion, among hemodialysis patients, although there is a U-shaped (paradoxical) association of dialysis-unit-SBP and risk of cardiovascular disease, there is a linear association of out-of-dialysis-unit-SBP with risk of cardiovascular disease. Out-of-dialysis-unit blood pressure provides key information and may be an important therapeutic target.

PMCID: PMC5521215 [Available on 2018-08-01] PMID: 28674037 [Indexed for MEDLINE] Hypertension. 2017 Sep;70(3):531-536.

Influence of Child and Adult Elevated Blood Pressure on Adult Arterial Stiffness: The Cardiovascular Risk in Young Finns Study.

Aatola H, Koivistoinen T, Tuominen H, Juonala M, Lehtimäki T, Viikari JSA, Raitakari OT, Kähönen M, Hutri-Kähönen N.

Elevated blood pressure (BP) in childhood has been associated with increased adult arterial stiffness, the independent predictor of cardiovascular and all-cause mortality. The favorable BP change from childhood to adulthood and the risk of high adult arterial stiffness has not been reported. We examined the effect of child and adult BP on pulse wave velocity (PWV) assessed in adulthood among 1540 white adults followed-up for 27 years since baseline (1980, aged 6-18 years). Childhood elevated BP was defined according to the tables from the National High Blood Pressure Education Program. In adulthood, BP was classified as elevated if systolic BP ≥120 mm Hg, diastolic BP ≥80 mm Hg, or selfreported use of antihypertensive medications. PWV was measured in 2007 by whole-body impedance cardiography, and high PWV was defined as values at or above the age-, sex-, and heart rate-specific 80th percentile. Individuals with persistently elevated BP and individuals with normal child but elevated adult BP had increased risk of high adult PWV (relative risk [95% confidence interval], 3.18 [2.22-4.55] and 2.64 [1.79-3.88], respectively) in comparison with individuals with normal (both child and adult) BP. In contrast, individuals with elevated BP in childhood but not in adulthood did not have significantly increased risk of high PWV (relative risk [95% confidence interval], 1.26[0.80-1.99]). The results were consistent when different definitions for child and adult elevated BP were applied. These findings highlight the importance of BP control in the primary prevention of cardiovascular diseases.

PMID: 28674036 [Indexed for MEDLINE]

Br J Nutr. 2017 Jun;117(11):1577-1586.

Dietary inflammatory index in relation to sub-clinical atherosclerosis and atherosclerotic vascular disease mortality in older women.

Bondonno NP, Lewis JR, Blekkenhorst LC, Shivappa N, Woodman RJ, Bondonno CP, Ward NC, Hébert JR, Thompson PL, Prince RL, Hodgson JM.

Arterial wall thickening, stimulated by low-grade systemic inflammation, underlies many cardiovascular events. As diet is a significant moderator of systemic inflammation, the dietary inflammatory index (DIITM) has recently been devised to assess the overall inflammatory potential of an individual's diet. The primary objective of this study was to assess the association of the DII with common carotid artery-intima-media thickness (CCA-IMT) and carotid plaques. To substantiate the clinical importance of these findings we assessed the relationship of DII score with atherosclerotic vascular disease (ASVD)-related mortality, ischaemic cerebrovascular disease (CVA)-related mortality and ischaemic heart disease (IHD)-related mortality more. The study was conducted in Western Australian women aged over 70 years (n 1304). Dietary data derived from a validated FFQ (completed at baseline) were used to calculate a DII score for each individual. In multivariable-adjusted models, DII scores were associated with sub-clinical atherosclerosis: a 1 sd (2.13 units) higher DII score was associated with a 0.013-mm higher mean CCA-IMT (P=0.016) and a 0.016-mm higher maximum CCA-IMT (P=0.008), measured at 36 months. No relationship was seen between DII score and carotid plaque severity. There were 269 deaths during follow-up. High DII scores were positively associated with ASVD-related death (per sd, hazard ratio (HR): 1·36; 95 % Cl 1·15, 1·60), CVA-related death (per sd, HR: 1·30; 95 % CI 1.00, 1.69) and IHD-related death (per sd, HR: 1.40; 95 % CI 1.13, 1.75). These results support the hypothesis that a pro-inflammatory diet increases systemic inflammation leading to development and progression of atherosclerosis and eventual ASVD-related death.

PMID: 28673375 [Indexed for MEDLINE]

Br J Nutr. 2017 Jul;118(2):144-153.

Association between spicy food consumption and lipid profiles in adults: a nationwide population-based study.

Xue Y, He T, Yu K, Zhao A, Zheng W, Zhang Y, Zhu B.

CVD remains the leading cause of mortality worldwide, with abnormal lipid metabolism as a major risk factor. The aim of this study was to investigate associations between spicy food consumption and serum lipids in Chinese adults. Data were extracted from the 2009 phase of the China Health and Nutrition Survey, consisting of 6774 apparently healthy Chinese adults aged 18-65 years. The frequency of consumption and degree of pungency of spicy food were self-reported, and regular spicy food consumption was assessed using three consecutive 24-h recalls. Total cholesterol, TAG, LDLcholesterol and HDL-cholesterol in fasting serum were measured. Multilevel mixed-effects models were constructed to estimate associations between spicy food consumption and serum lipid profiles. The results showed that the frequency and the average amount of spicy food intake were both inversely associated with LDL-cholesterol and LDL-cholesterol:HDL-cholesterol ratio (all P for trend<0.05) after adjustment for potential confounders and cluster effects. HDL-cholesterol in participants who usually consumed spicy food (>5 times/week) and who consumed spicy food perceived as moderate in pungency were significantly higher than those who did not (both P<0.01). The frequency and the average amount of spicy food intake and the degree of pungency in spicy food were positively associated with TAG (all P for trend<0.05). Spicy food consumption was inversely associated with serum cholesterol and positively associated with serum TAG, and additional studies are needed to confirm the findings as well as to elucidate the potential roles of spicy food consumption in lipid metabolism.

PMID: 28673367 [Indexed for MEDLINE]

Nutr Metab Cardiovasc Dis. 2017 Aug;27(8):695-702.

Muscular fitness, adherence to the Southern European Atlantic Diet and cardiometabolic risk factors in adolescents.

Agostinis-Sobrinho C, Abreu S, Moreira C, Lopes L, García-Hermoso A, Ramírez-Vélez R, Correa-Bautista JE, Mota J, Santos R.

BACKGROUND AND AIM: Muscular fitness and an adherence to the Southern European Atlantic Diet (SEADiet) have been inversely associated with cardiometabolic risk. Our aim was to assess the independent and combined associations of muscular fitness and adherence to the SEADiet on cardiometabolic risk in adolescents.

METHODS AND RESULTS: A total of 467 Portuguese adolescents (275 girls) participated in this cross-sectional study. Sum of the Z-Scores of Curl-Up and Push-Up tests was used to create a muscular fitness score. Adherence to SEADiet was obtained using a food frequency questionnaire. A cardiometabolic risk score was computed from sum of Z-score of triglycerides, systolic blood pressure, total cholesterol/HDL ratio, HOMA-IR and waist circumference. Adolescents with low muscular fitness and low adherence to the SEADiet had the poorest cardiovascular profile F(5, 452) = 5.074 (p < 0.001) and the highest odds of having a high cardiometabolic risk score (OR = 4.5; 95% CI: 2.1-14) when compared to those with High muscular fitness/High adherence to the SEADiet after adjustments for age, sex, pubertal stage, socioeconomic status, total energy intake, low-energy reporter and cardiorespiratory fitness.

CONCLUSIONS: Our findings seem suggest that improving muscular fitness as well as an adherence to the SEADiet could be an important strategy to reduce clustered cardiometabolic risk in youth.

PMID: 28669448 [Indexed for MEDLINE]

Can J Cardiol. 2017 Jul;33(7):947-949.

Modifiable Risk Factors in Atrial Fibrillation: The Role of Alcohol, Obesity, and Sleep Apnea.

Sidhu K, Tang A.

Atrial fibrillation (AF) is a common arrhythmia affecting a growing number of Canadians. Traditional risk factors, such as hypertension, diabetes, and valvular disease, are often present in older patients with AF. Modifiable risk factors should also be sought in patients presenting with new-onset AF. Obesity is a rapidly growing epidemic in Canada. Emerging evidence is linking obesity and the often coexistent obstructive sleep apnea with an increased incidence of AF. Alcohol intake can also predispose to the development of AF. The purpose of this article is to review recent evidence looking at these modifiable risk factors and how intervention can mitigate these increased risks.

PMID: 28668145 [Indexed for MEDLINE]

Nat Rev Endocrinol. 2017 Sep;13(9):547-560.

Type 2 diabetes mellitus and psychological stress - a modifiable risk factor.

Hackett RA, Steptoe A.

Psychological stress is common in many physical illnesses and is increasingly recognized as a risk factor for disease onset and progression. An emerging body of literature suggests that stress has a role in the aetiology of type 2 diabetes mellitus (T2DM) both as a predictor of new onset T2DM and as a prognostic factor in people with existing T2DM. Here, we review the evidence linking T2DM and psychological stress. We highlight the physiological responses to stress that are probably related to T2DM, drawing on evidence from animal work, large epidemiological studies and human laboratory trials. We discuss population and clinical studies linking psychological and social stress factors with T2DM, and give an overview of intervention studies that have attempted to modify psychological or social factors to improve outcomes in people with T2DM.

PMID: 28664919 [Indexed for MEDLINE]

Hypertension. 2017 Aug;70(2):285-292.

Cardiovascular Health and Incident Hypertension in Blacks: JHS (The Jackson Heart Study).

Booth JN 3rd, Abdalla M, Tanner RM, Diaz KM, Bromfield SG, Tajeu GS, Correa A, Sims M, Ogedegbe G, Bress AP, Spruill TM, Shimbo D, Muntner P.

Several modifiable health behaviors and health factors that comprise the Life's Simple 7-a cardiovascular health metric-have been associated with hypertension risk. We determined the association between cardiovascular health and incident hypertension in JHS (the Jackson Heart Study)-a cohort of blacks. We analyzed participants without hypertension or cardiovascular disease at baseline (2000-2004) who attended ≥1 follow-up visit in 2005 to 2008 or 2009 to 2012 (n=1878). Body mass index, physical activity, diet, cigarette smoking, blood pressure (BP), total cholesterol, and fasting glucose were assessed at baseline and categorized as ideal, intermediate, or poor using the American Heart Association's Life's Simple 7 definitions. Incident hypertension was defined at the first visit wherein a participant had systolic BP ≥140 mm Hg, diastolic BP ≥90 mm Hg, or self-reported taking antihypertensive medication. The percentage of participants with ≤1, 2, 3, 4, 5, and 6 ideal Life's Simple 7 components was 6.5%, 22.4%, 34.4%, 25.2%, 10.0%, and 1.4%, respectively. No participants had 7 ideal components. During follow-up (median, 8.0 years), 944 (50.3%) participants developed hypertension, including 81.3% with ≤1 and 11.1% with 6 ideal components. The multivariable-adjusted hazard ratios (95% confidence interval) for incident hypertension comparing participants with 2, 3, 4, 5, and 6 versus ≤1 ideal component were 0.80 (0.61-1.03), 0.58 (0.45-0.74), 0.30 (0.23-0.40), 0.26 (0.18-0.37), and 0.10 (0.03-0.31), respectively (Ptrend < 0.001). This association was present among participants with baseline systolic BP <120 mm Hg and diastolic BP <80 mm Hg and separately systolic BP 120 to 139 mm Hg or diastolic BP 80 to 89 mm Hg. Blacks with better cardiovascular health have lower hypertension risk.

PMID: 28652461 [Indexed for MEDLINE]

J Am Coll Cardiol. 2017 Jul 11;70(2):123-132.

Knowledge, Attitudes, and Beliefs Regarding Cardiovascular Disease in Women: The Women's Heart Alliance.

Bairey Merz CN, Andersen H, Sprague E, Burns A, Keida M, Walsh MN, Greenberger P, Campbell S, Pollin I, McCullough C, Brown N, Jenkins M, Redberg R, Johnson P, Robinson B.

BACKGROUND: Cardiovascular disease (CVD) is the number 1 killer of women in the United States, yet few younger women are aware of this fact. CVD campaigns focus little attention on physicians and their roles in assessing risk.

OBJECTIVES: In 2014, the Women's Heart Alliance (WHA) conducted a nationwide survey to determine barriers and opportunities for women and physicians with regard to CVD.

METHODS: From September 18 to 26, 2014, a total of 1,011 U.S. women (age 25 to 60 years) were interviewed using the GfK ("Gesellschaft für Konsumforschung" Knowledge Panel). From May 6 to 12, 2014, the e-Rewards Inc. Physician and Healthcare Professional Panel surveyed 200 primary care physicians (PCPs) and 100 cardiologists.

RESULTS: Overall, 45% of women were unaware that CVD is the number 1 killer of women; only 11% knew a woman who died from CVD. Overall, 45% of women reported it was common to cancel or postpone a physician appointment until losing weight. CVD was rated as the top concern by only 39% of PCPs, after weight and breast health. Only 22% of PCPs and 42% of cardiologists (p = 0.0477) felt extremely well prepared to assess CVD risk in women, while 42% and 40% felt well-prepared (p = NS), respectively. Few comprehensively implemented guidelines.

CONCLUSIONS: CVD was rated as the top concern less frequently than weight issues by both women and physicians. Social stigma particularly regarding body weight appeared to be a barrier. Physicians reported limited training and use of guideline assessment, whereas most supported a campaign and improved physician education. Campaigns should make CVD "real" to U.S. women, countering stereotypes with facts and validated assessments. Both community women and physicians endorsed investment in women's CVD research and physician education.

PMID: 28648386 [Indexed for MEDLINE]

Circulation. 2017 Aug 29;136(9):798-812.

Incident Cardiovascular Disease Among Adults With Blood Pressure <140/90 mm Hg.

Tajeu GS, Booth JN 3rd, Colantonio LD, Gottesman RF, Howard G, Lackland DT, O'Brien EC, Oparil S, Ravenell J, Safford MM, Seals SR, Shimbo D, Shea S, Spruill TM, Tanner RM, Muntner P.

BACKGROUND: Data from before the 2000s indicate that the majority of incident cardiovascular disease (CVD) events occur among US adults with systolic and diastolic blood pressure (SBP/DBP) ≥140/90 mmHg. Over the past several decades, BP has declined and hypertension control has improved.

METHODS: We estimated the percentage of incident CVD events that occur at SBP/DBP <140/90 mmHg in a pooled analysis of 3 contemporary US cohorts: the REGARDS study (Reasons for Geographic and Racial Differences in Stroke), the MESA (Multi-Ethnic Study of Atherosclerosis), and the JHS (Jackson Heart Study) (n=31856; REGARDS=21208; MESA=6779; JHS=3869). Baseline study visits were conducted in 2003 to 2007 for REGARDS, 2000 to 2002 for MESA, and 2000 to 2004 for JHS. BP was measured by trained staff using standardized methods. Antihypertensive medication use was self-reported. The primary outcome was incident CVD, defined by the first occurrence of fatal or nonfatal stroke, nonfatal myocardial infarction, fatal coronary heart disease, or heart failure. Events were adjudicated in each study.

RESULTS: Over a mean follow-up of 7.7 years, 2584 participants had incident CVD events. Overall, 63.0% (95% confidence interval [CI], 54.9-71.1) of events occurred in participants with SBP/DBP <140/90 mmHg; 58.4% (95% CI, 47.7-69.2) and 68.1% (95% CI, 60.1-76.0) among those taking and not taking antihypertensive medication, respectively. The majority of events occurred in participants with SBP/DBP <140/90 mmHg among those <65 years of age (66.7%; 95% CI, 60.5-73.0) and \geq 65 years of age (60.3%; 95% CI, 51.0-69.5), women (61.4%; 95% CI, 49.9-72.9) and men (63.8%; 95% CI, 58.4-69.1), and for whites (68.7%; 95% CI, 66.1-71.3), blacks (59.0%; 95% CI, 49.5-68.6), Hispanics (52.7%; 95% CI, 45.1-60.4), and Chinese-Americans (58.5%; 95% CI, 45.2-71.8). Among participants taking antihypertensive medication with SBP/DBP <140/90 mmHg, 76.6% (95% CI, 75.8-77.5) were eligible for statin treatment, but only 33.2% (95% CI, 32.1-34.3) were taking one, and 19.5% (95% CI, 18.5-20.5) met the SPRINT (Systolic Blood Pressure Intervention Trial) eligibility criteria and may benefit from a SBP target goal of 120 mmHg.

CONCLUSIONS: Although higher BP levels are associated with increased CVD risk, in the modern era, the majority of incident CVD events occur in US adults with SBP/DBP <140/90 mmHg. While absolute risk and cost-effectiveness should be considered, additional CVD risk-reduction measures for adults with SBP/DBP <140/90 mmHg at high risk for CVD may be warranted.

PMCID: PMC5580500 [Available on 2018-08-29] PMID: 28634217 [Indexed for MEDLINE] Stroke. 2017 Jul;48(7):1744-1751.

Contribution of Established Stroke Risk Factors to the Burden of Stroke in Young Adults.

Aigner A(Grittner U, Rolfs A, Norrving B, Siegerink B, Busch MA.

BACKGROUND AND PURPOSE: As stroke in young adults is assumed to have different etiologies and risk factors than in older populations, the aim of this study was to examine the contribution of established potentially modifiable cardiovascular risk factors to the burden of stroke in young adults. METHODS: A German nationwide case-control study based on patients enrolled in the SIFAP1 study (Stroke In Young Fabry Patients) 2007 to 2010 and controls from the population-based GEDA study (German Health Update) 2009 to 2010 was performed. Cases were 2125 consecutive patients aged 18 to 55 years with acute first-ever stroke from 26 clinical stroke centers; controls (age- and sexmatched, n=8500, without previous stroke) were from a nationwide community sample. Adjusted population-attributable risks of 8 risk factors (hypertension, hyperlipidemia, diabetes mellitus, coronary heart disease, smoking, heavy episodic alcohol consumption, low physical activity, and obesity) and their combinations for all stroke, ischemic stroke, and primary intracerebral hemorrhage were calculated.

RESULTS: Low physical activity and hypertension were the most important risk factors, accounting for 59.7% (95% confidence interval, 56.3-63.2) and 27.1% (95% confidence interval, 23.6-30.6) of all strokes, respectively. All 8 risk factors combined explained 78.9% (95% confidence interval, 76.3-81.4) of all strokes. Population-attributable risks of all risk factors were similar for all ischemic stroke subtypes. Population-attributable risks of most risk factors were higher in older age groups and in men.

CONCLUSIONS: Modifiable risk factors previously established in older populations also account for a large part of stroke in younger adults, with 4 risk factors explaining almost 80% of stroke risk.

CLINICAL TRIAL REGISTRATION: URL: http://www.clinicaltrials.gov. Unique identifier: NCT00414583.

PMID: 28619986 [Indexed for MEDLINE]

Am J Clin Nutr. 2017 Jul;106(1):27-34.

Dietary calcium intake and risk of cardiovascular disease, stroke, and fracture in a population with low calcium intake.

Kong SH, Kim JH, Hong AR, Cho NH, Shin CS.

Background: The role of dietary calcium intake in cardiovascular disease (CVD), stroke, and fracture is controversial. Most previous reports have evaluated populations with high calcium intake.

Objective: We aimed to evaluate whether high dietary calcium intake was associated with the risk of CVD, stroke, and fracture in a population with low calcium intake.

Design: In a prospective cohort study beginning in 2001 in Ansung-Ansan, Korea, 2158 men and 2153 women aged >50 y were evaluated for all-cause mortality, CVD, stroke, and fractures over a median 9-y follow-up.

Results: During follow-up, 242 and 100 deaths, 149 and 150 CVD events, 58 and 82 stroke events, and 211 and 292 incident fractures occurred in men and women, respectively. The first quartiles of energy-adjusted dietary calcium intake were 249 mg/d (IQR: 169 mg/d) in men and 209 mg/d (IQR: 161 mg/d) in women. Both men and women with higher dietary calcium intake tended to have higher fat, protein, sodium, phosphorus, fruit, and vegetable intakes. In men, outcomes were not significantly associated with dietary calcium intake with or without adjustments, and CVD risk tended to increase with increasing energy-adjusted dietary calcium intake, but this was not statistically significant (P = 0.078 and P = 0.093 with and without adjustment, respectively). In women, CVD risk and dietary calcium intake showed a U-shaped association; the HRs (95% CIs) without adjustment relative to the first quartile were 0.71 (0.47, 1.07), 0.57 (0.36, 0.88), and 0.52 (0.33, 0.83) for quartiles 2, 3, and 4, respectively, and the values after adjustment were 0.70 (0.45, 1.07), 0.51 (0.31, 0.81), and 0.49 (0.29, 0.83) for quartiles 2, 3, and 4, respectively.

Conclusion: In Korean women, increased dietary calcium intake was associated with a decreased CVD risk, but it did not influence the risk of stroke or fracture.

PMID: 28615253 [Indexed for MEDLINE]

JAMA Intern Med. 2017 Aug 1;177(8):1165-1172.

Association of Educational Attainment With Lifetime Risk of Cardiovascular Disease: The Atherosclerosis Risk in Communities Study.

Kubota Y, Heiss G, MacLehose RF, Roetker NS, Folsom AR.

Importance: Estimates of lifetime risk may help raise awareness of the extent to which educational inequalities are associated with risk of cardiovascular disease (CVD).

Objective: To estimate lifetime risks of CVD according to categories of educational attainment.

Design, Setting, and Participants: Participants were followed from 1987 through December 31, 2013. All CVD events (coronary heart disease, heart failure, and stroke) were confirmed by physician review and International Classification of Diseases codes. A total of 13 948 whites and African Americans who were 45 to 64 years old and free of CVD at baseline were included from 4 US communities (Washington County, Maryland; Forsyth County, North Carolina; Jackson, Mississippi; and suburbs of Minneapolis, Minnesota). The data analysis was performed from June 7 to August 31, 2016. Exposures: Educational attainment.

Main Outcomes and Measures: We used a life table approach to estimate lifetime risks of CVD from age 45 through 85 years according to educational attainment. We adjusted for competing risks of death from underlying causes other than CVD.

Results: The sample of 13 948 participants was 56% female and 27% African American. During 269 210 person-years of follow-up, we documented 4512 CVD events and 2401 non-CVD deaths. Educational attainment displayed an inverse dose-response relation with cumulative risk of CVD, which became evident in middle age, with the most striking gap between those not completing vs completing high school. In men, lifetime risks of CVD were 59.0% (95% CI, 54.0%-64.1%) for grade school, 52.5% (95% CI, 47.7%-56.8%) for high school education without graduation, 50.9% (95% CI, 47.3%-53.9%) for high school graduation, 47.2% (95% CI, 41.5%-52.5%) for vocational school, 46.4% (95% CI, 42.8%-49.6%) for college with or without graduation, and 42.2% (95% CI, 36.6%-47.0%) for graduate/professional school; in women, 50.8% (95% CI, 45.7%-55.8%), 49.3% (95% CI, 45.1%-53.1%), 36.3% (95% CI, 21.9%-33.3%), respectively. Educational attainment was inversely associated with CVD even within categories of family income, income change, occupation, or parental educational level.

Conclusions and Relevance: More than 1 in 2 individuals with less than high school education had a lifetime CVD event. Educational attainment was inversely associated with the lifetime risk of CVD, regardless of other important socioeconomic characteristics. Our findings emphasize the need for further efforts to reduce CVD inequalities related to educational disparities.

PMID: 28604921 [Indexed for MEDLINE]

Am J Clin Nutr. 2017 Jul;106(1):207-216.

Association of dietary nitrate with atherosclerotic vascular disease mortality: a prospective cohort study of older adult women.

Blekkenhorst LC, Bondonno CP, Lewis JR, Devine A, Woodman RJ, Croft KD, Lim WH, Wong G, Beilin LJ, Prince RL, Hodgson JM.

Background: Nitrate-rich vegetables lower blood pressure and improve endothelial function in humans. It is not known, however, whether increased consumption of nitrate-rich vegetables translates to a lower risk of atherosclerotic vascular disease (ASVD) mortality.

Objective: The objective was to investigate the association of nitrate intake from vegetables with ASVD mortality.Design: A total of 1226 Australian women aged 70-85 y without prevalent ASVD and/or diabetes were recruited in 1998 and were studied for 15 y. We assessed demographic and ASVD risk factors at baseline (1998), and we used a validated food-frequency questionnaire to evaluate dietary intake. Nitrate intake from vegetables was calculated by use of a newly developed comprehensive database. The primary outcome was any death attributed to ASVD ascertained by using linked data that were provided via the Western Australian Data Linkage system. We used Cox proportional hazards modeling to examine the association between nitrate intake and ASVD mortality before and after adjustment for lifestyle and cardiovascular disease risk factors.

Results: During a follow-up period of 15,947 person-years, 238 of 1226 (19.4%) women died of ASVDrelated causes. The mean \pm SD vegetable nitrate intake was 67.0 \pm 29.2 mg/d. Each SD higher vegetable nitrate intake was associated with a lower risk of ASVD mortality in both unadjusted [HR: 0.80 (95% CI: 0.70, 0.92), P = 0.002] and multivariable-adjusted [HR: 0.79 (95% CI: 0.68, 0.93), P = 0.004] analyses. This relation was attenuated after further adjustment for diet quality [HR: 0.85 (95% CI: 0.72, 1.01), P = 0.072]. Higher vegetable nitrate intake (per SD) also was associated with a lower risk of all-cause mortality [multivariable-adjusted HR: 0.87 (95% CI: 0.78, 0.97), P = 0.011].

Conclusions: Nitrate intake from vegetables was inversely associated with ASVD mortality independent of lifestyle and cardiovascular disease risk factors in this population of older adult women without prevalent ASVD or diabetes. These results support the concept that nitrate-rich vegetables may reduce the risk of age-related ASVD mortality. This trial was registered at www.anzctr.org.au as ACTRN12617000640303.

PMID: 28566306 [Indexed for MEDLINE]

Hypertension. 2017 Jul;70(1):103-110.

Risk of Cardiovascular Events in Patients With Diabetes Mellitus on β -Blockers.

Tsujimoto T, Sugiyama T, Shapiro MF, Noda M, Kajio H.

Although the use of β-blockers may help in achieving maximum effects of intensive glycemic control because of a decrease in the adverse effects after severe hypoglycemia, they pose a potential risk for the occurrence of severe hypoglycemia. This study aimed to evaluate whether the use of β -blockers is effective in patients with diabetes mellitus and whether its use is associated with the occurrence of severe hypoglycemia. Using the ACCORD trial (Action to Control Cardiovascular Risk in Diabetes) data, we performed Cox proportional hazards analyses with a propensity score adjustment. The primary outcome was the first occurrence of a cardiovascular event during the study period, which included nonfatal myocardial infarction, unstable angina, nonfatal stroke, and cardiovascular death. The mean follow-up periods (\pm SD) were 4.6 \pm 1.6 years in patients on β -blockers (n=2527) and 4.7 \pm 1.6 years in those not on β -blockers (n=2527). The cardiovascular event rate was significantly higher in patients on β -blockers than in those not on β -blockers (hazard ratio, 1.46; 95% confidence interval, 1.24-1.72; P<0.001). In patients with coronary heart disease or heart failure, the cumulative event rate for cardiovascular events was also significantly higher in those on β -blockers than in those not on β blockers (hazard ratio, 1.27; 95% confidence interval, 1.02-1.60; P=0.03). The incidence of severe hypoglycemia was significantly higher in patients on β-blockers than in those not on β-blockers (hazard ratio, 1.30; 95% confidence interval, 1.03-1.64; P=0.02).

In conclusion, the use of β -blockers in patients with diabetes mellitus was associated with an increased risk for cardiovascular events.

PMID: 28559400 [Indexed for MEDLINE]

Environ Res. 2017 Aug;157:110-117.

Traffic noise and hypertension - results from a large case-control study.

Zeeb H, Hegewald J, Schubert M, Wagner M, Dröge P, Swart E, Seidler A.

BACKGROUND: Environmental traffic noise is a potential cause of hypertension. We aimed to study the association between hypertension as recorded in health insurance claims data and the exposure to three sources of traffic noise (aircraft, road and rail).

METHODS: This large case-control study was conducted among persons aged 40 and above in 2010 and living in the region around Frankfurt airport in Germany. Individual residential noise exposure for the index year 2005 was assessed using standard noise algorithms. Cases were all newly diagnosed cases of hypertension recorded in three large health insurances databases in the period 2006-2010.

Controls had no hypertension diagnosis. Categorical and continuous analyses were conducted with binary logistic regression models adjusted for sex, age and residential area-based socioeconomic information.

RESULTS: The main analysis included 137,577 cases and 355,591 controls. There were no associations with any of the traffic noise sources. Odds ratios (OR) per 10dB noise increase were 0.99 (95% confidence interval: 0.98;1.01) for aircraft noise, and 1.00 (0.99;1.01) both for road and railway noise. Similarly, nighttime noise levels showed no associations with hypertension. Odds ratios were increased for the subgroup of newly diagnosed hypertension cases with a subsequent diagnosis of hypertensive heart disease: per 10dB aircraft noise there was a 13.9% OR increase (6.0% for road traffic, 5.4% for rail traffic). Increases were also noted when we analyzed cases with a longer exposure-outcome time window.

CONCLUSION: Our results are suggestive of an association of noise exposure with clinically more severe hypertension diagnoses, but not with uncomplicated hypertension. The absence of individual confounder data, however, adds to the risk of bias. The results contribute to evidence on traffic noise as a cardiovascular risk factor.

PMID: 28554004 [Indexed for MEDLINE]

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Risk Factors for Recurrent Cardiovascular Events Before Age 65 Years or Within 2.5 Years of a Recent First Cardiovascular Event.

van den Berg MJ, Westerink J, van der Graaf Y, Kappelle LJ, de Borst GJ, Cramer MM, Visseren FLJ; SMART study group.

The aim of this study was to quantify the relation between classical risk factors (smoking, diabetes, BMI, waist circumference, blood pressure, and lipids), risk factor targets, and risk of recurrent major atherosclerotic cardiovascular events (MACE). This was first done for recurrent MACE ≤65 years in patients aged <60 years and second for recurrent MACE ≤2.5 years after a first cardiovascular event. Data were used from the Second Manifestations of Arterial Disease study (n = 5,115), a prospective cohort of patients with a recent (≤1 year) first cardiovascular event. During follow-up, 746 recurrent MACE occurred. Smoking (hazard ratio [HR] 1.43, 95% CI 1.11 to 1.84), diabetes (HR 1.83, 95% CI 1.11 to 1.84), diastolic blood pressure (>90 vs 70 to 90 mm Hg, HR 1.54, 95% CI 1.15 to 2.07), and high-density lipoprotein cholesterol (≤1.0 vs >1.0 mmol/L, HR 1.34, 95% CI 1.03 to 1.76) were related to increased risk of recurrent MACE ≤65 years in patients aged <60 years. Smoking (HR 1.65, 95% CI 1.23 to 2.22), physical inactivity (highest vs lowest tertile, HR 1.48, 95% CI 1.05 to 2.09), body mass index (per kg/m(2), HR 1.04, 95% CI 1.00 to 1.08), diastolic blood pressure (>90 vs 70 to 90 mm Hg, HR 1.61, 95% CI 1.17 to 2.21), low-density lipoprotein cholesterol (per mmol/L, HR 1.18, 95% CI 1.02 to 1.37), and non-high-density lipoprotein cholesterol (per mmol/L, HR 1.15, 95% CI 1.03 to 1.28) were related to recurrent MACE ≤2.5 years of follow-up. In conclusion, in patients with a recent cardiovascular event, smoking, blood pressure, and lipids are related to increased risk of recurrent cardiovascular events at young age or within a short time span, and intensive treatment of modifiable risk factors may contribute to prevent recurrent MACE in these patients.

PMID: 28532782 [Indexed for MEDLINE]

J Am Coll Cardiol. 2017 Jul 4;70(1):1-25.

Global, Regional, and National Burden of Cardiovascular Diseases for 10 Causes, 1990 to 2015.

Roth GA, et al

BACKGROUND: The burden of cardiovascular diseases (CVDs) remains unclear in many regions of the world.

OBJECTIVES: The GBD (Global Burden of Disease) 2015 study integrated data on disease incidence, prevalence, and mortality to produce consistent, up-to-date estimates for cardiovascular burden.

METHODS: CVD mortality was estimated from vital registration and verbal autopsy data. CVD prevalence was estimated using modeling software and data from health surveys, prospective cohorts, health system administrative data, and registries. Years lived with disability (YLD) were estimated by multiplying prevalence by disability weights. Years of life lost (YLL) were estimated by multiplying age-specific CVD deaths by a reference life expectancy. A sociodemographic index (SDI) was created for each location based on income per capita, educational attainment, and fertility.

RESULTS: In 2015, there were an estimated 422.7 million cases of CVD (95% uncertainty interval: 415.53 to 427.87 million cases) and 17.92 million CVD deaths (95% uncertainty interval: 17.59 to 18.28 million CVD deaths). Declines in the age-standardized CVD death rate occurred between 1990 and 2015 in all high-income and some middle-income countries. Ischemic heart disease was the leading cause of CVD health lost globally, as well as in each world region, followed by stroke. As SDI increased beyond 0.25, the highest CVD mortality shifted from women to men. CVD mortality decreased sharply for both sexes in countries with an SDI >0.75.

CONCLUSIONS: CVDs remain a major cause of health loss for all regions of the world. Sociodemographic change over the past 25 years has been associated with dramatic declines in CVD in regions with very high SDI, but only a gradual decrease or no change in most regions. Future updates of the GBD study can be used to guide policymakers who are focused on reducing the overall burden of noncommunicable disease and achieving specific global health targets for CVD.

PMCID: PMC5491406 PMID: 28527533 [Indexed for MEDLINE] Am J Clin Nutr. 2017 Jul;106(1):35-43.

Low-fat dietary pattern and cardiovascular disease: results from the Women's Health Initiative randomized controlled trial.

Prentice RL, Aragaki AK, Van Horn L, Thomson CA, Beresford SA, Robinson J, Snetselaar L, Anderson GL, Manson JE, Allison MA, Rossouw JE, Howard BV.

Background: The influence of a low-fat dietary pattern on the cardiovascular health of postmenopausal women continues to be of public health interest.

Objective: This report evaluates low-fat dietary pattern influences on cardiovascular disease (CVD) incidence and mortality during the intervention and post-intervention phases of the Women's Health Initiative Dietary Modification Trial.

Design: Participants comprised 48,835 postmenopausal women aged 50-79 y; 40% were randomly assigned to a low-fat dietary pattern intervention (target of 20% of energy from fat), and 60% were randomly assigned to a usual diet comparison group. The 8.3-y intervention period ended in March 2005, after which >80% of surviving participants consented to additional active follow-up through September 2010; all participants were followed for mortality through 2013. Breast and colorectal cancer were the primary trial outcomes, and coronary heart disease (CHD) and overall CVD were additional designated outcomes.

Results: Incidence rates for CHD and total CVD did not differ between the intervention and comparison groups in either the intervention or post-intervention period. However, CHD HRs comparing these groups varied strongly with baseline CVD and hypertension status. Participants without prior CVD had an intervention period CHD HR of 0.70 (95% CI: 0.56, 0.87) or 1.04 (95% CI: 0.90, 1.19) if they were normotensive or hypertensive, respectively (P-interaction = 0.003). The CHD benefit among healthy normotensive women was partially offset by an increase in ischemic stroke risk. Corresponding HRs in the post-intervention period were close to null. Participants with CVD at baseline (3.4%) had CHD HRs of 1.47 (95% CI: 1.12, 1.93) and 1.61 (95% CI: 1.02, 2.55) in the intervention and post-intervention periods, respectively. However, various lines of evidence suggest that results in women with CVD or hypertension at baseline are confounded by post-randomization use of cholesterol-lowering medications.

Conclusions: CVD risk in postmenopausal women appears to be sensitive to a change to a low-fat dietary pattern and, among healthy women, includes both CHD benefit and stroke risk. This trial was registered at clinicaltrials.gov as NCT00000611.

PMCID: PMC5486201 [Available on 2018-07-01] PMID: 28515068 [Indexed for MEDLINE] Laryngoscope. 2017 Aug;127(8):1742-1745.

Smoking: An independent risk factor for lost productivity in chronic rhinosinusitis.

Campbell AP, Hoehle LP, Phillips KM, Caradonna DS, Gray ST, Sedaghat AR(1)(2)(3)(4).

OBJECTIVES/HYPOTHESIS: Chronic rhinosinusitis (CRS) is associated with a significant loss of patient productivity that costs billions of dollars every year. Smoking is associated with worsening sinonasal symptoms, but its effect on lost productivity in CRS patients has yet to be described. Therefore, we sought to determine the association between smoking and productivity in patients with CRS.

STUDY DESIGN: Prospective cross-sectional cohort study of 140 patients with CRS.

METHODS: Sinonasal symptom severity was measured using the 22-item Sino-Nasal Outcomes Test. Lost productivity was assessed by asking participants how many days of work and/or school they missed in the last 3 months due to CRS. Associations were sought between lost productivity and smoking.

RESULTS: Participants missed a mean of 3.0 days (standard deviation = 12.8 days) of work or school due to CRS. Having any history of smoking was associated with 6 days of lost productivity due to CRS (adjusted β = 6.20, 95% confidence interval [CI]: 0.64 to 11.77, P = .031). Although the number of active smokers in our study cohort was very small (N = 6), we performed a univariate association between smoking status, considering former smokers and active smokers separately, and found that active smoking (β = 11.75, 95% CI: 2.11 to 21.40, P = .018) had a much larger impact on CRS-related productivity loss than that experienced by former smokers (β = 4.45, 95% CI: -0.32 to 9.23, P = .070). CONCLUSIONS: Smoking (likely driven by active smoking) is independently associated with missed days of work or school in patients with CRS. Further study is needed to determine whether interventions directed at smoking may impact CRS-related productivity loss.

LEVEL OF EVIDENCE: 2c Laryngoscope, 127:1742-1745, 2017.

PMID: 28295361 [Indexed for MEDLINE]

J Am Geriatr Soc. 2017 Sep;65(9):1907-1915.

Body Mass Index, Waist Circumference, and Mortality in a Large Multiethnic Postmenopausal Cohort-Results from the Women's Health Initiative.

Chen Z, Klimentidis YC, Bea JW, Ernst KC, Hu C, Jackson R, Thomson CA.

OBJECTIVES: To determine whether the relationship between anthropometric measurements of obesity and mortality varies according to age, race, and ethnicity in older women.

DESIGN: Prospective cohort study of multiethnic postmenopausal women.

SETTING: Women's Health Initiative (WHI) observational study and clinical trials in 40 clinics.

PARTICIPANTS: Postmenopausal women aged 50-79 participating in WHI (N = 161,808).

MEASUREMENTS: Baseline height, weight, and waist circumference (WC) were measured, and body mass index (BMI) was calculated based on height and weight. Demographic, health, and lifestyle data from a baseline questionnaire were used as covariates. The outcome was adjudicated death (n = 18,320) during a mean follow-up of 11.4 ± 3.2 years.

RESULTS: Hazard ratios (HRs) and 95% confidence intervals (95% CIs) indicated that ethnicity and age modified (P < .01) the relationship between obesity and mortality. Underweight was associated with higher mortality, but overweight or slight obesity was not a risk factor for mortality in most ethnic groups except for Hispanic women in the obesity I category (HR = 1.42, 95% CI = 1.04-1.95). BMI was not or was only weakly associated with mortality in individuals aged 70-79 (HR = 0.90, 95% CI = 0.85-0.95 for overweight; HR = 0.98, 95 CI = 0.92-1.06 for obese I; HR = 1.11, 95% CI = 1.00-1.23 for obese II; HR = 1.08, 95% CI = 0.92-1.26 for obese III). In contrast, higher central obesity measured using WC was consistently associated with higher mortality in all groups.

CONCLUSION: Underweight is a significant risk factor for mortality in older women, and healthy BMI ranges may need to be specific for age, race, and ethnicity. The findings support a consistent relationship between central obesity and mortality.

PMCID: PMC5569001 [Available on 2018-09-01] PMID: 28229456 [Indexed for MEDLINE] Rheumatology (Oxford). 2017 Sep 1;56(9):1472-1478.

Cardiovascular risk management in rheumatoid arthritis patients still suboptimal: the Implementation of Cardiovascular Risk Management in Rheumatoid Arthritis project.

van den Oever IAM, Heslinga M, Griep EN, Griep-Wentink HRM, Schotsman R, Cambach W, Dijkmans BAC, Smulders YM, Lems WF, Boers M, Voskuyl AE, Peters MJL, van Schaardenburg D, Nurmohamed MT.

Objective: To assess the 10-year cardiovascular (CV) risk score and to identify treatment and undertreatment of CV risk factors in patients with established RA.

Methods: Demographics, CV risk factors and prevalence of cardiovascular disease (CVD) were assessed by questionnaire. To calculate the 10-year CV risk score according to the Dutch CV risk management guideline, systolic blood pressure was measured and cholesterol levels were determined from fasting blood samples. Patients were categorized into four groups: indication for treatment but not treated; inadequately treated, so not meeting goals (systolic blood pressure \leq 140 mmHg and/or low-density lipoprotein \leq 2.5 mmol/l); adequately treated; or no treatment necessary.

Results: A total of 720 consecutive RA patients were included, 375 from Reade and 345 from the Antonius Hospital. The mean age of patients was 59 years (s.d. 12) and 73% were female. Seventeen per cent of the patients had a low 10-year CV risk (<10%), 21% had an intermediate risk (10-19%), 53% a high risk (\geq 20%) and 9% had CVD. In total, 69% had an indication for preventive treatment (cholesterol-lowering or antihypertensive drugs). Of those, 42% received inadequate treatment and 40% received no treatment at all.

Conclusion: Optimal CV risk management remains a major challenge and better awareness and management are urgently needed to reduce the high risk of CVD in the RA population.

PMID: 28199724 [Indexed for MEDLINE]

Chest. 2017 Aug;152(2):435-444.

Insomnia and Risk of Cardiovascular Disease.

Javaheri S, Redline S.

Insomnia is the most prevalent sleep disorder in the United States and has high comorbidity with a number of cardiovascular diseases (CVDs). In the past decade, a number of observational studies have demonstrated an association between insomnia and incident cardiovascular disease (CVD) morbidity and mortality, including hypertension (HTN), coronary heart disease (CHD), and heart failure (HF). Despite some inconsistencies in the literature, likely due to variations in how insomnia is defined and measured, the existing data suggest that insomnia, especially when accompanied by short sleep duration, is associated with increased risk for HTN, CHD and recurrent acute coronary syndrome, and HF. Purported mechanisms likely relate to dysregulation of the hypothalamic-pituitary axis, increased sympathetic nervous system activity, and increased inflammation. This paper reviews the most recent studies of insomnia and CVD and the potential pathophysiological mechanisms underlying this relationship and highlights the need for randomized trials to further elucidate the nature of the relationship between insomnia and CVD.

PMCID: PMC5577359 [Available on 2018-08-01] PMID: 28153671 [Indexed for MEDLINE] Ann Rheum Dis. 2017 Jul;76(7):1263-1268.

Cardiovascular risk of patients with gout seen at rheumatology clinics following a structured assessment.

Andrés M, Bernal JA, Sivera F, Quilis N, Carmona L, Vela P, Pascual E.

OBJECTIVES: Gout-associated cardiovascular (CV) risk relates to comorbidities and crystal-led inflammation. The aim was to estimate the CV risk by prediction tools in new patients with gout and to assess whether ultrasonographic carotid changes are present in patients without high CV risk.

METHODS: Cross-sectional study. Consecutive new patients with crystal-proven gout underwent a structured CV consultation, including CV events, risk factors and two risk prediction tools-the Systematic COronary Evaluation (SCORE) and the Framingham Heart Study (FHS). CV risk was stratified according to current European guidelines. Carotid ultrasound (cUS) was performed in patients with less than very high CV risk. The presence of carotid plaques was studied depending on the SCORE and FHS by the area under the curve (AUC) of receiver operating curves.

RESULTS: 237 new patients with gout were recruited. CV stratification by scores showed a predominance of very high (95 patients, 40.1%) and moderate (72 patients, 30.5%) risk levels. cUS was performed in 142 patients, finding atheroma plaques in 66 (46.5%, 95% CI 37.8 to 54.2). Following cUS findings, patients classified as very high risk increased from 40.1% up to 67.9% (161/237 patients). SCORE and FHS predicted moderately (AUC 0.711 and 0.683, respectively) the presence of atheroma plaques at cUS.

CONCLUSIONS: The majority of patients presenting with gout may be at very high CV risk, indicating the need for initiating optimal prevention strategies at this stage. Risk prediction tools appear to underestimate the presence of carotid plaque in patients with gout.

PMID: 28093417 [Indexed for MEDLINE]

J Gerontol A Biol Sci Med Sci. 2017 Jul 1;72(7):958-964.

Cardiovascular Dysfunction and Frailty Among Older Adults in the Community: The ARIC Study.

Nadruz W Jr, Kitzman D, Windham BG, Kucharska-Newton A, Butler K, Palta P, Griswold ME, Wagenknecht LE, Heiss G, Solomon SD, Skali H, Shah AM.

Background: The contribution of cardiovascular dysfunction to frailty in older adults is uncertain. This study aimed to define the relationship between frailty and cardiovascular structure and function, and determine whether these associations are independent of coexisting abnormalities in other organ systems.

Methods: We studied 3,991 older adults (mean age 75.6 \pm 5.0 years; 59% female) from the Atherosclerosis Risk in Communities (ARIC) Study in whom the following six organ systems were uniformly assessed: cardiac (by echocardiography), vascular (by ankle-brachial-index and pulse-wave-velocity), pulmonary (by spirometry), renal (by estimated glomerular filtration rate), hematologic (by hemoglobin), and adipose (by body mass index and bioimpedance). Frailty was defined by the presence of \geq 3 of the following: low strength, low energy, slowed motor performance, low physical activity, or unintentional weight loss.

Results: Two hundred eleven (5.3%) participants were frail. In multivariable analyses adjusted for demographics, diabetes, hypertension, and measures of other organ system function, frailty was independently and additively associated with left ventricular hypertrophy (odds ratio [OR] = 1.72; 95% confidence interval [CI] = 1.30-2.40), reduced global longitudinal strain (reflecting systolic function; OR = 1.68; 95% CI = 1.16-2.44), and greater left atrial volume index (reflecting diastolic function; OR = 1.60; 95% CI = 1.13-2.27), which together demonstrated the greatest association with frailty (OR = 2.10; 95% CI = 1.57-2.82) of the systems studied. Lower magnitude associations were observed for vascular and pulmonary abnormalities, anemia, and impaired renal function. Cardiovascular abnormalities remained associated with frailty after excluding participants with prevalent cardiovascular disease.

Conclusions: Abnormalities of cardiac structure and function are independently associated with frailty, and together show the greatest association with frailty among the organ systems studied.

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Validation of a pharmacological model for mitochondrial dysfunction in healthy subjects using simvastatin: A randomized placebocontrolled proof-of-pharmacology study.

van Diemen MPJ, Berends CL, Akram N et al

The statin related muscle side effects have been linked to impaired mitochondrial function caused by a depletion of downstream metabolites in the cholesterol synthesis pathway. In this experimental design study healthy volunteers were treated with simvastatin 40 mg for 8 weeks. After 4 weeks subjects were randomized to ubiquinol (Co-enzyme Q10) 300mg/day. Mitochondrial (dys)function was evaluated by measuring phosphocreatine recovery time (τ -PCr) using phosphorous Magnetic Resonance Spectroscopy (31PMRS) after in-magnet exercise. All participants showed a mean increase in τ -PCr of 15.2% (2.5–29.4%; P = 0.018), compared to baseline. At study completion the τ -PCr further increased in the placebo group: 37.27 s; a mean increase of 18.5% (1.1–38.9%; P = 0.037). In the ubiquinol group there was an attenuated increase in τ -PCr of 33.81 s; a mean increase of 9.1% (–7.9 to 29.2%; P = 0.31). In the placebo group the τ -PCr was significantly different from baseline at 8 weeks. No difference between baseline and 8 weeks measurements in the active treatment arm. The observed τ -PCr difference between the two groups was not statistical significant, 8.2% (–14.5 to 37.0%; P = 0.51). The authors concluded that simvastatin treatment can impair mitochondrial function even in healthy subjects and this attenuation can be partly reversed by ubiquinone 300 mg/day treatment.

Therapy in Patients With Low Serum Levels of Low-Density Lipoprotein Cholesterol.

Tsujimoto T, Kajio H, Sugiyama T. Statin

Using data collected in the Japanese National Health and Nutrition Examination Survey 1999–2010, 1 500 high CVD-risk patients with LDL-c levels < 120 mg/dl (mean LDL-c 88.7 mg/dl) were evaluated. Using a Cox proportional hazards models unadjusted and multivariable-adjusted hazard ratios were calculated. There was a significant lower risk in patients using statins for all-cause mortality; HR: 0.62 (0.45-0.85; P=0.004). Patients with LDL-c <100 mg/dl the risk for total mortality was significantly reduced as well; HR: 0.50 (0.34-0.74; P=0.001). In patients with LDL-c <70mg/dl no significant difference was observed when compared to patients with LDL-c 70-120 mg/dl; HR 1.27 (0.72-2.10; P=0.35). Patients with moderately to high risk of CVD showed similar outcomes. Despite the limitations of the observational design of this study, the robustness of the collected data and the use of various statistical analyses makes a good case for initiating statin treatment in patients with an LDL-C <120 mg/dl but moderate to high CVD risk. Therefore, the authors emphasized the need for of large-scale and long-term follow-up studies and RCTs to confirm the results of the present study.

High-sensitivity C-reactive protein levels and health status outcomes after myocardial infarction.

Pokharel Y, Sharma PP, Qintar M et al.

The role of hsCRP as a risk predictor has been controversial with a greater acceptance in North America and more skepticism in Europe. The recently published CANTOS trial rekindled the debate on the role of hsCRP in CVD risk. In this article the role of hsCRP not only as a risk marker but its association with health status is examined in 3 410 post AMI patients. Using data collected in two large prospective US - AMI registries, TRIUMPH (N=1301) and VIRGO (N=2109). Patients with elevated hsCRP (>2 mg/dl) were compared with those that had a low hsCRP (<2mg/dl). The 30-day hsCRP levels were compared with the 1-year health status (based on 3 validated questionnaires). Most patients (92%) were using statins after hospital discharge and the median 30-day hs CRP levels was 2.6 mg/dl (25th and 95th percentile: 1.1-6.1 mg/dl). In the un-adjusted and partly-adjusted models (based on co-morbidities) the 30-day hsCRP> 2mg/dl was inversely related to 1-year health status. No significant difference was observed in the fully-adjusted model. Based on this finding the authors concluded that hs-CRP is a marker of co-morbidities associated with worse health status one year after AMI. If reduction of hs-CRP – inflammation will improve health status needs to be evaluated in trials that exclusively target inflammation like the CANTOS study and ongoing studies that are using low dose methotrexate and colchicine.

A population-based cohort study on the drug specific effect of statins on sepsis outcome.

Lee CC, Lee MG, Hsu TC et al

The potential benefits of statins in serious life-threatening conditions like sepsis is discussed in this retrospective observational Taiwanese study using data collected in the National Health Insurance Research Database (2001 - 2011). Data from 53 737 of sepsis patients were appraised. Patient included were using statins >30 day prior to the sepsis admission (n=3 598) and only patients that were using atorvastatin (N=1 855), rosuvastatin (N=732) and simvastatin (N=916) were entered. Sepsis outcome was evaluated by using a Cox model and a propensity score (PS) matched model. The latter by using 1:1:1 PS matching technique. When comparing the patients not using statins with simvastatin and atorvastatin their respective HR's for the primary endpoint of this study, the 30-day survival, improved; HR: 0.72, (0.58-0.90) and HR: 0.78 (0.68-0.90) respectively. The survival benefits at 90 days were somewhat attenuated but remained significant. This was not observed in patients using rosuvastatin; HR: 0.87 (0.73-1.04). When applying rosuvastatin as the reference population both atorvastatin: HR 0.79 (0.64-0.99) and simvastatin: HR 0.77 (0.59-0.99) showed a better survival. The authors suggest that non-lipid lowering effects of statins are responsible for the observed improved survival. In experimental, animal studies preservation of cardiac function, attenuation of inflammatory cytokines and neutrophil infiltration in the lung and inhibiting T-cell dysfunction were observed. Atorvastatin, pravastatin, rosuvastatin but particular simvastatin seem to have direct anti-microbial and anti-virulence effects as well, that could contribute and to some extend explain the observed benefits.

Regional Evidence and International Recommendations to Guide Lipid Management in Asian Patients with Type 2 Diabetes with Special Reference to Renal Dysfunction.

Lau TW, Tan KE, Choo JC et al.

This review by one of Hong Kong's leading diabetologists, Julia Chan aims to addresses the anticipated increase in the prevalence and incidence of DM2 in Asia. The combined cardio-renal organ complications observed in diabetics will create a tremendous strain on the health care system and will have serious health budget consequences as well. The emphasis of recent guidelines to initiate lipid lowering treatment solely based on absolute risk estimation, instead of LDL-C targets, has not been widely implemented in clinical practice. Especially in patients with diabetes, reflecting very high CVD risk, treatment strategies should facilitate starting early with guideline indicated medications. In Asian diabetic patients the risk of developing renal disease seems to be enhanced and the augmented effects on ASCVD puts an even greater emphasis on using the appropriate statin (high intensity) and (high) dose. Of note, due to the difference in drug metabolism observed in Asian patients, rosuvastatin should be prescribed in low dosages (5-10 mg) in patients of this ethnic background. The authors prioritize the use of moderate- to high-intensity statins such as simvastatin 20-40 mg and Atorvastatin 10-40 mg. Atorvastatin based on the proven safety in Asian populations plus the pleiotropic and organ protective effects, as shown in epidemiological and experimental studies as well as the recent UK NICE guidelines, is an attractive (first) choice. Having a pro-active lipid management approach in Asian diabetic patients can have a significant impact in reducing diabetes CKD and ASCVD related complications. A simple and cost-effective strategy to reduce the substantial burden of diabetes in Asia.

The effect of lipophilicity and dose on the frequency of statinassociated muscle symptoms: A systematic review and meta-analysis.

Irwin JC, Khalesi S, Fenning AS, Vella RK.

In this article the authors pondered the question if statin lipophilicity as compared to hydrophilicity, could help us to better understand the statin associated muscle symptoms (SAMS) phenomenon. They conducted a meta-analysis according to the universally accepted PRISMA guidelines. From the initial 5 545 studies 135 RCT's were included in this meta-analysis, 129 had parallel and 6 a cross-over design. Sixteen trials were not double blinded and in 86 stated that they were randomized, but the method of sequence generation for randomization was not provided. In total 192 977 patients were treated with statins and 92 546 received placebo or usual care. Adverse muscle symptoms were observed in 8 755 statin treated patients and 7 885 placebo/usual care participants. Statin use showed a small risk increase for SAMS compared to placebo RR = 1.050 (1.014-1.089; P = 0.007). No additional risk for the use of lipophilic statins compared to hydrophilic statins or high dose compared to lows dose could be determined. In the overall analysis the increased risk of SAMS in statin users were mostly observed in patients with a history of statin intolerance. The authors concluded that there was very limited evidence pointing towards an increases SAMS risk in patients using lipophilic and/or high dose as compared to hydrophilic and low dose statins.