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Pesquisa Bibliográfica efectuada em Pubmed (www.ncbi.nlm.nih.gov/ -Outl a Dezt 2018

Crit Rev Oncol Hematol. 2019 Jan;133:129-141

Metabolic syndrome as cardiovascular risk factor in childhood cancer survivors.

Pluimakers VG, van Waas M, Neggers SJCMM, van den Heuvel-Eibrink MM.

Over the past decades, survival rates of childhood cancer have increased considerably from 5 to 30% in the early seventies to current rates exceeding 80%. This is due to the development of effective chemotherapy, surgery, radiotherapy and stem cell transplantation, combined with an optimized stratification of therapy and better supportive care regimens. As a consequence, active surveillance strategies of late sequelae have been developed to improve the quality of survival. Several epidemiological studies have reported an increased incidence of (components of) metabolic syndrome (MetS) and cardiovascular disease in childhood cancer survivors (CCS). Growth hormone deficiency (GHD) after cranial radiotherapy (CRT) has been previously described as an important cause of MetS. New insights suggest a role for abdominal radiotherapy as a determinant for MetS as well. The role of other risk factors, such as specific chemotherapeutic agents, steroids, gonadal impairment, thyroid morbidity and genetics, warrants further investigation. This knowledge is important to define subgroups of CCS that are at risk to develop (subclinical) MetS features. These survivors might benefit from standard surveillance and early interventions, for example lifestyle and diet advice and medical treatment, thereby preventing the development of cardiovascular disease.

PMID: 30661649

JAMA Netw Open. 2018 Nov 2;1(7):e183788.

Association Between Obesity and Cardiovascular Outcomes: A Systematic Review and Meta-analysis of Mendelian Randomization Studies.

Riaz H, Khan MS, Siddiqi TJ, Usman MS, Shah N, Goyal A, Khan SS, Mookadam F, Krasuski RA, Ahmed H.

Importance: Although dyslipidemia has been consistently shown to be associated with atherogenesis, an association between obesity and cardiovascular disease outcomes remains controversial. Mendelian randomization can minimize confounding if variables are randomly and equally distributed in the population of interest. Objective: To assess evidence from mendelian randomization studies to provide a less biased estimate of any association between obesity and cardiovascular outcomes.

Data Sources: Systematic searches of MEDLINE and Scopus from database inception until January 2018, supplemented with manual searches of the included reference lists. Study Selection: Studies that used mendelian randomization methods to assess the association between any measure of obesity and the incidence of cardiovascular events and those that reported odds ratios (ORs) with 95% CIs estimated using an instrumental variable method were included. The 5 studies included in the final analysis were based on a consensus among 3 authors.

Data Extraction and Synthesis: Two in vestigators independently extracted study characteristics using a standard form and pooled data using a random-effects model. The Meta-analysis of Observational Studies in Epidemiology (MOOSE) reporting guideline was followed.

Main Outcomes and Measures: Obesity associated with type 2 diabetes, coronary artery disease, or stroke. The hypothesis was formulated prior to data collection. Results: Of 4660 potentially relevant articles, 2511 titles were screened. Seven studies were included in the systematic review, and 5 studies with 881 692 participants were eligible to be included in the meta-analysis. Pooled estimates revealed that obesity was significantly associated with an increased risk of type 2 diabetes (OR, 1.67; 95% CI, 1.30-2.14; P < .001; I2 = 93%) and coronary artery disease (OR, 1.20; 95% CI, 1.02-1.41; P = .03; I2 = 87%). No association between obesity and stroke was found (OR, 1.02; 95% CI, 0.95-1.09; P = .65; I2 = 0%).

Conclusions and Relevance: The present meta-analysis suggests that obesity is associated with type 2 diabetes and coronary artery disease. Although this analysis of mendelian randomization studies does not prove causality, it is supportive of a causal association. Hence, health care practitioners should continue to emphasize weight reduction to combat coronary artery disease.

PMID: 30646365

Diabetes Metab Syndr. 2019 Jan - Feb;13(1):866-872.

High prevalence of prediabetes among the family members of individuals with diabetes. Findings from targeted screening program from south India.

Ramaswamy G, Chinnakali P, Selvaraju S, Nair D, Thekkur P, Selvaraj K, Shivashankar R, Singh AR, Vrushabhendra HN.

AIM: We aimed to screen for prediabetes, diabetes and other cardiovascular risk factors among family members of people with diabetes registered for care in a primary health centre in South India.

METHODS: During 2017-2018, we screened eligible family members of individuals with diabetes at their homes. We measured fasting capillary blood glucose (FCBG); for those with FCBG≥126 mg/dl, we confirmed the diagnosis of diabetes with fasting plasma glucose (FPG). We defined prediabetes as FCBG between 100 and 125 mg/dl; diabetes as both FCBG and FPG ≥126 mg/dl. We assessed non-communicable disease risk factors using WHO STEPS questionnaire.

RESULTS: Of total 884 participants, 873 (99%) underwent screening; 280 (32%) had prediabetes, and 19 (2.2%) were confirmed with diabetes. Of newly diagnosed, 17 (90%) were initiated on treatment. Of 873 participants, 180 (20.6%) were newly diagnosed with hypertension. Of the total, 7.3%, 5.2% and 16% reported tobacco use, alcohol use and high salt intake respectively. Nearly half (48%) had overweight.

CONCLUSION: Though the yield for diabetes is modest (3%), the house to house approach was able to screen 99% of eligible population. High prevalence of prediabetes and undiagnosed hypertension emphasize the need for screening and life style modifications.

PMID: 30641823

Atherosclerosis. 2018 Dec 7;281:25-30.

Lipoprotein(a) as a risk factor for calcific aortic valvulopathy in heterozygous familial hypercholesterolemia.

Vuorio A, Watts GF, Kovanen PT.

A large number of epidemiological studies in ethnically diverse populations show that lipoprotein(a) [Lp(a)] levels above 30-50 mg/dL are significantly associated with calcific aortic valve stenosis, although less so in African Americans. Patients with heterozygous familial hypercholesterolemia (he-FH) have a marked lifelong elevation of serum low-density lipoprotein cholesterol (LDL-C) level, and the prevalence of aortic valve calcification (AVC) is at least two-fold higher among adult he-FH patients compared with healthy controls. Additionally, Lp(a) levels above 50 mg/dL were recently found to be an independent risk factor for AVC among asymptomatic statin-treated he-FH patients. Given that worldwide an estimated 1.4 billion people have an Lp(a) level over 50 mg/dL, and that one out of 250 individuals has he-FH, then globally about 5 million he-FH patients should have an Lp(a) level higher than 50 mg/dL. However, because Lp(a) levels are, on average, significantly higher in he-FH patients than the general population, the actual number of he-FH patients with such high Lp(a) levels must be even higher. We proposed recently that Lp(a) life-years is a useful metric of cumulative burden of risk for atherosclerotic cardiovascular disease (ASCVD), and now posit that this metric may be extended to the development of AVC. The Lp(a) life-years illustrates the age-dependent exposure to a given Lp(a) level (years x mg/dL). Effective novel pharmacotherapies using apo(a) antisense oligonucleotides (ASOs) or small interfering RNA (siRNA)-based therapies targeting the hepatic expression of apo(a) offer unprecedented potential for significant reduction in the cumulative exposure of the aortic valves to Lp(a), and need to be tested in controlled clinical trials on the progression of AVC.

PMID: 30616181

J Am Heart Assoc. 2018 Nov 6;7(21):e010019.

Circulating Very Long-Chain Saturated Fatty Acids and Heart Failure: The Cardiovascular Health Study.

Lemaitre RN, McKnight B, Sotoodehnia N, Fretts AM, Qureshi WT, Song X, King IB, Sitlani CM, Siscovick DS, Psaty BM, Mozaffarian D.

Background: Circulating very-long-chain saturated fatty acids (VLSFAs) are integrated biomarkers of diet and metabolism that may point to new risk pathways and potential targets for heart failure (HF) prevention. The associations of VLSFA to HF in humans are not known. Methods and Results: Using a cohort study design, we studied the associations of serially measured plasma phospholipid VLSFA with incident HF in the Cardiovascular Health Study. We investigated the associations of time-varying levels of the 3 major circulating VLSFAs , lignoceric acid (24:0), behenic acid (22:0), and arachidic acid (20:0), with the risk of incident HF using Cox regression. During 45030 person-years among 4249 participants, we identified 1304 cases of incident HF, including 489 with preserved and 310 with reduced ejection fraction. Adjusting for major HF risk factors and other circulating fatty acids, higher levels of each VLSFAs were associated with lower risk of incident HF (P trend≤0.0007 each). The hazard ratio comparing the highest quintile to the lowest quintile was 0.67 (95% confidence interval, 0.55-0.81) for 24:0, 0.72 (95% confidence interval, 0.60-0.87) for 22:0 and 0.72 (95% confidence interval, 0.59-0.88) for 20:0. The associations were similar in subgroups defined by sex, age, body mass index, coronary heart disease, and diabetes mellitus. Among those with ejection fraction data, the associations appeared similar for those with preserved and with reduced ejection fraction.
Conclusions: Higher levels of circulating VLSFAs are associated with lower risk of incident HF in older adults. These novel associations should prompt further research on the role of VLSFA in HF, including relevant new risk pathways.

Clinical Trial Registration URL : https://www.clinicaltrials.gov .
Unique identifier: NCT 00005133.

PMID: 30608197

Circulation. 2018 Nov 26. [Epub ahead of print]

Glycemic Control, Cardiac Autoimmunity, and Long-Term Risk of Cardiovascular Disease in Type 1 Diabetes Mellitus: A DCCT/EDIC Cohort-Based Study.

Sousa GR, Pober D, Galderisi A, Lv H, Yu L, Pereira AC, Doria A, Kosiborod M, Lipes MA.

BACKGROUND: Poor glycemic control is associated with increased risk of cardiovascular disease (CVD) in type 1 diabetes mellitus (T1DM); however, little is known about mechanisms specific to T1DM. In T1DM, myocardial injury can induce persistent cardiac autoimmunity. Chronic hyperglycemia causes myocardial injury, raising the possibility that hyperglycemia-induced cardiac autoimmunity could contribute to long-term CVD complications in T1DM.
METHODS: We measured the prevalence and profiles of cardiac autoantibodies (AAbs) in longitudinal samples from the DCCT (Diabetes Control and Complications Trial) in participants with mean hemoglobin A1c (HbA1c) ≥9.0% (n=83) and ≤7.0% (n=83) during DCCT. We assessed subsequent coronary artery calcification (measured once during years 7-9 in the post-DCCT EDIC [Epidemiology of Diabetes Interventions and Complications] observational study), high-sensitivity C-reactive protein (measured during EDIC years 4-6), and CVD events (defined as nonfatal myocardial infarction, stroke, death resulting from CVD, heart failure, or coronary artery bypass graft) over a 26-year median followup. Cardiac AAbs were also measured in matched patients with type 2 diabetes mellitus with HbA1c ≥9.0% (n=70) and ≤7.0% (n=140) and, as a control for cardiac autoimmunity, patients with Chagas cardiomyopathy (n=51).
RESULTS: Apart from HbA1c levels, the DCCT groups shared similar CVD risk factors at the beginning and end of DCCT. The DCCT HbA1c ≥9.0% group showed markedly higher cardiac AAb levels than the HbA1c ≤7.0% group during DCCT, with a progressive increase and decrease in AAb levels over time in the 2 groups, respectively (P<0.001). In the HbA1c ≥9.0% group, 46%, 22%, and 11% tested positive for ≥1, ≥2, and ≥3 different cardiac AAb types, respectively, similar to patients with Chagas cardiomyopathy, compared with 2%, 1%, and 0% in the HbA1c ≤7.0% group. Glycemic control was not associated with AAb prevalence in type 2 diabetes mellitus. Positivity for ≥2 AAbs during DCCT was associated with increased risk of CVD events (4 of 6; hazard ratio, 16.1; 95% CI, 3.0-88.2) and, in multivariable analyses, with detectable coronary artery calcification (13 of 31; odds ratio, 60.1; 95% CI, 8.4-410.0). Patients with ≥2 AAbs subsequently also showed elevated high-sensitivity C-reactive protein levels (6.0 mg/L versus 1.4 mg/L in patients with ≤1 AAbs; P=0.003). CONCLUSIONS: Poor glycemic control is associated with cardiac autoimmunity in T1DM. Furthermore, cardiac AAb positivity is

associated with an increased risk of CVD decades later, suggesting a role for autoimmune mechanisms in the development of CVD in T1DM, possibly through inflammatory pathways.

PMID: 30586738

Nutrients. 2018 Dec 22;11(1). pii: E31. doi: 10.3390/nu11010031.

Effects of Consuming Calcium-Rich Foods on the Incidence of Type 2 Diabetes Mellitus.

Jeon J, Jang J, Park K.

The effect of calcium consumption in the prevention of type 2 diabetes mellitus (T2DM) remains controversial, and depends on food calcium sources. This prospective study aimed to evaluate the association between calcium-rich food consumption and T2DM incidence among Korean adults. We analyzed the data of 8574 adults aged 40⁻69 years, without a history of T2DM, cardiovascular disease, and cancer at the baseline from the Korean Genome and Epidemiology Study. The consumption of calcium-rich foods was assessed using a validated semi-quantitative food frequency questionnaire. T2DM-related data were collected using biennial questionnaires, health examinations, and clinical tests. Hazard ratios (HRs) and 95% confidence intervals (CIs) were calculated using Cox proportional hazards regression models. In the multivariate-adjusted model, yogurt intake was inversely associated with T2DM risk (HR: 0.73; 95% CI: 0.61⁻0.88 in the fourth quartile as compared to the first quartile). However, the intakes of other calcium-rich foods, including milk and anchovies, were not significantly associated with T2DM risk. Yogurt may provide protective effects against T2DM in Korean adults, owing to the beneficial effects of probiotics. Further prospective large-scale cohort studies should be conducted to validate these findings.

PMID: 30583546

JRSM Cardiovasc Dis. 2018 Dec 12;7:2048004018818923.

Why are there ethnic differences in cardio-metabolic risk factors and cardiovascular diseases?

Dal Canto E, Farukh B, Faconti L.

Europe's population is becoming increasingly ethnically diverse, and epidemiological studies indicate that there are remarkable differences in cardio-metabolic risk factors between ethnic groups living in the same area. Variations observed in the distribution of cardiovascular risk factors in these communities may therefore help explain-at least in part-the different burdens on cardiovascular diseases. So far, the underlying pathophysiology leading to ethnic variations in the prevalence of cardio-metabolic risk factors is still poorly understood but it is likely to represent the complex interactions from several innate and environmental factors. Tailored prevention and treatment strategies should therefore be implemented in those "high-risk populations," but data derived from randomized clinical trials are still limited. This article will provide an overview on the role of ethnicity on cardio-metabolic risk factors and cardiovascular diseases, focusing on type 2 diabetes and dyslipidemia based mainly on Dutch and British data.

PMCID: PMC6299297
PMID: 30574299

Nutrients. 2018 Dec 19;10(12). pii: E2012.

Erythrocyte n-6 Fatty Acids and Risk for Cardiovascular Outcomes and Total Mortality in the Framingham Heart Study.

Harris WS, Tintle NL, Ramachandran VS.

BACKGROUND: The prognostic value of erythrocyte levels of n-6 fatty acids (FAs) for total mortality and cardiovascular disease (CVD) outcomes remains an open question.
METHODS: We examined cardiovascular (CV) outcomes and death in 2500 individuals in the Framingham Heart Study Offspring cohort without prevalent CVD (mean age 66 years, 57% women) as a function of baseline levels of different length n-6 FAs (18 carbon, 20 carbon, and 22 carbon) in the erythrocyte membranes. Clinical outcomes were monitored for up to 9.5 years (median follow up, 7.26 years). Cox proportional hazards models were adjusted for a variety of demographic characteristics, clinical status, and red blood cell (RBC) n-6 and long chain n-3 FA content.
RESULTS: There were 245 CV events, 119 coronary heart disease (CHD) events, 105 ischemic strokes, 58 CVD deaths, and 350 deaths from all causes. Few associations between either mortality or CVD outcomes were observed for n-6 FAs, with those that were observed becoming non-significant after adjusting for n-3 FA levels.
CONCLUSIONS: Higher circulating levels of marine n-3 FA levels are associated with reduced risk for incident CVD and ischemic stroke and for death from CHD and all-causes; however, in the same sample little evidence exists for association with n-6 FAs. Further work is needed to identify a full profile of FAs associated with cardiovascular risk and mortality.

PMCID: PMC6316092
PMID: 30572606

Curr Med Chem. 2018 Dec 19. [Epub ahead of print]

Cardiovascular effects of flavonoids.

Sanchez M, Romero M, Gómez-Guzman M, Tamargo J, Pérez-Vizcaino F, Duarte J.

Cardiovascular disease (CVD) is the major cause of death worldwide, especially in Western society. Flavonoids are a large group of polyphenolic compounds widely distributed in plants, present in considerable amount in fruit and vegetable. Several epidemiological studies found an inverse association between flavonoids intake and mortality by CVD. The antioxidant effect of flavonoids was considered the main mechanism of action of flavonoids and other polyphenols. In recent years, the role of modulation of signaling pathways by direct interaction of flavonoids with multiple protein targets, namely kinases, has been increasingly recognized and involved in their cardiovascular protective effect. There are strong evidences, in in vitro and animal experimental models, that some flavonoids induce vasodilator effects, improve endothelial dysfunction and insulin resistance, exert platelet antiaggregant and atheroprotective effects, and reduce blood pressure. Despite interacting with multiple targets, flavonoids are surprisingly safe. This article reviews the recent evidences about cardiovascular effects that support a beneficial role of flavonoids on CVD and the potential molecular targets involved.

PMID: 30569843

Br J Sports Med. 2018 Dec 15. pii: bjsports-2018-099740 . [Epub ahead of print]

Physical activity less than the recommended amount may prevent the onset of major biological risk factors for cardiovascular disease: a cohort study of 198919 adults.

Martinez-Gomez D, Esteban-Cornejo I, Lopez-Garcia E, García-Esquinas E, Sadarangani KP, Veiga OL, Rodriguez-Artalejo F.

OBJECTIVES: We examined the dose-response relationship between physical activity (PA) and incidence of cardiovascular disease (CVD) risk factors in adults in Taiwan.
METHODS: This study included 198919 participants, aged 18-97 years, free of CVD, cancer and diabetes at baseline (1997-2013), who were followed until 2016. At baseline, participants were classified into five PA levels: inactive' (0 metabolic equivalent of task (MET)-h/week), 'lower insufficiently active' (0.1-3.75 MET-h/week), 'upper insufficiently active' (3.75-7.49 MET-h/week), 'active' (7.5-14.99 MET-h/week) and 'highly active' (≥15 MET-h/week]. CVD risk factors were assessed at baseline and at follow-up by physical examination and laboratory tests. Analyses were performed with Cox regression and adjusted for the main confounders.
RESULTS: During a mean follow-up of 6.0±4.5 years (range 0.5-19 years), 20447 individuals developed obesity, 19619 hypertension, 21592 hypercholesterolaemia, 14164 atherogenic dyslipidaemia, 24275 metabolic syndrome and 8548 type 2 diabetes. Compared with inactive participants, those in the upper insufficiently active (but not active) category had a lower risk of obesity (HR 0.92; 95% CI 0.88 to 0.95), atherogenic dyslipidaemia (0.96; 0.90 to 0.99), metabolic syndrome (0.95; 0.92 to 0.99) and type 2 diabetes (0.91; 0.86 to 0.97). Only highly active individuals showed a lower incidence of CVD risk factors than their upper insufficiently active counterparts.
CONCLUSION: Compared with being inactive, doing half the recommended amount of PA is associated with a lower incidence of several common biological CVD risk factors. Given these benefits, half the recommended amount of PA is an evidence based target for inactive adults.

PMID: 30554146

Clin Chim Acta. 2018 Dec 13;490:1-5.

Remnant lipoproteins and atherosclerotic cardiovascular disease.

Tada H, Nohara A, Inazu A, Mabuchi H, Kawashiri MA.

Lipoproteins are one of the major risk factors for atherosclerotic cardiovascular disease (ASCVD), among which, low-density lipoprotein (LDL) particles have been definitively shown to be causally associated with the development of ASCVD. Additionally, the concept of remnant lipoproteins has emerged as lipoprotein metabolism has been fully investigated. The principal concept of this lipoprotein category is triglyceride-rich lipoproteins significantly increase at the postprandial state. Although there is no clear definition of remnant lipoproteins, they typically include chylomicron remnants, which are lipolyzed particles from chylomicron, as well as very low-density lipoprotein (VLDL) and intermediate-density lipoprotein (IDL) remnants that are lipolyzed particles from VLDL and IDL particles. However, the most important factor of these lipoproteins is such remnant lipoproteins seem to be causally associated with ASCVD, independent of LDL particles or LDL cholesterol. It has been challenging to assert a causal association of remnant lipoproteins and ASCVD; however, accumulated evidence from epidemiological studies, as well as recent Mendelian randomization studies from common and rare genetic variations strongly support this association. In this article, a basic explanation of lipoprotein metabolism is presented, including remnant lipoproteins and the important causal associations with ASCVD from a clinical point of view.

PMID: 30553862

Eur J Epidemiol. 2019 Jan;34(1):37-55.

Cardiovascular mortality attributable to dietary risk factors in 51 countries in the WHO European Region from 1990 to 2016: a systematic analysis of the Global Burden of Disease Study.

Meier T, Gräfe K, Senn F, Sur P, Stangl GI, Dawczynski C, März W, Kleber ME, Lorkowski S.

This study was performed to highlight the relationship between single dietary risk factors and cardiovascular diseases (CVDs) in the WHO European Region. We used the comparative risk assessment framework of the Global Burden of Disease Study to estimate CVD mortality attributable to diet; comprising eleven forms of CVDs, twelve food and nutrient groups and 27 risk-outcome pairs in four GBD regions including 51 countries by age and sex between 1990 and 2016. In 2016, dietary risks were associated with 2.1 million cardiovascular deaths (95% uncertainty interval (UI), 1.7-2.5 million) in the WHO European Region, accounting for 22.4% of all deaths and 49.2% of CVD deaths. In terms of single dietary risks, a diet low in whole grains accounted for approximately 429,000 deaths, followed by a diet low in nuts and seeds (341,000 deaths), a diet low in fruits (262,000 deaths), a diet high in sodium (251,000 deaths), and a diet low in omega-3 fatty acids (227,000 deaths). Thus, with an optimized, i.e. balanced diet, roughly one in every five premature deaths could be prevented. Although age-standardized death rates decreased over the last 26 years, the absolute number of diet-related cardiovascular deaths increased between 2010 and 2016 by 25,600 deaths in Western Europe and by 4300 deaths in Central Asia. In 2016, approximately 601,000 deaths (28.6% of all diet-related CVD deaths) occurred among adults younger than 70 years. Compared to other behavioural risk factors, a balanced diet is a potential key lever to avoid premature deaths.

PMID: 30547256

J Am Coll Cardiol. 2018 Dec 11;72(23 Pt B):2951-2963

Reprint of: Cardiovascular Disease Prevention by Diet Modification: JACC Health Promotion Series.

Yu E, Malik VS, Hu FB.

Reduction in excess calories and improvement in dietary composition may prevent many primary and secondary cardiovascular events. Current guidelines recommend diets high in fruits, vegetables, whole grains, nuts, and legumes; moderate in low-fat dairy and seafood; and low in processed meats, sugar-sweetened beverages, refined grains, and sodium. Supplementation can be useful for some people but cannot replace a good diet. Factors that influence individuals to consume a low-quality diet are myriad and include lack of knowledge, lack of availability, high cost, time scarcity, social and cultural norms, marketing of poor-quality foods, and palatability. Governments should focus on cardiovascular disease as a global threat and enact policies that will reach all levels of society and create a food environment wherein healthy foods are accessible, affordable, and desirable. Health professionals should be proficient in basic nutritional knowledge to promote a sustainable pattern of healthful eating for cardiovascular disease prevention for both healthy individuals and those at higher risk.

PMID: 30522630

Heart. 2018 Dec 11. pii: heartjnl-2018-313463. [Epub ahead of print]

Association of occupational exposures with cardiovascular disease among US Hispanics/Latinos.

Bulka CM, Daviglus ML, Persky VW, Durazo-Arvizu RA, Lash JP, Elfassy T, Lee DJ, Ramos AR, Tarraf W, Argos M.

OBJECTIVE: Cardiovascular disease (CVD) is a leading cause of mortality and morbidity in the USA. The role of occupational exposures to chemicals in the development of CVD has rarely been studied even though many agents possess cardiotoxic properties. We therefore evaluated associations of self-reported exposures to organic solvents, metals and pesticides in relation to CVD prevalence among diverse Hispanic/Latino workers.
METHODS: Cross-sectional data from 7404 employed individuals, aged 18-74 years, enrolled in the Hispanic Community Health Study/Study of Latinos (HCHS/SOL) were analysed. Participants from four US cities provided questionnaire data and underwent clinical examinations, including ECGs. CVD was defined as the presence of at least one of the following: coronary heart disease, atrial fibrillation, heart failure or cerebrovascular disease. Prevalence ratios reflecting the relationship between each occupational exposure and CVD as well as CVD subtypes were calculated using Poisson regression models.
RESULTS: Hispanic/Latino workers reported exposures to organic solvents (6.5%), metals (8.5%) and pesticides (4.7%) at their current jobs. Overall, 6.1% of participants had some form of CVD, with coronary heart disease as the most common (4.3%) followed by cerebrovascular disease (1.0%), heart failure (0.8%) and atrial fibrillation (0.7%). For individuals who reported working with pesticides, the prevalence ratios for any CVD were 2.18 (95% CI 1.34 to 3.55), coronary heart disease 2.20 (95% CI 1.31 to 3.71), cerebrovascular disease 1.38 (95% CI 0.62 3.03), heart failure 0.91 (95% CI 0.23 to 3.54) and atrial fibrillation 5.92 (95% CI 1.89 to 18.61) after adjustment for sociodemographic, acculturation, lifestyle and occupational characteristics. Metal exposures were associated with an almost fourfold (3.78, 95% CI 1.24 to 11.46) greater prevalence of atrial fibrillation. Null associations were observed for organic solvent exposures.
CONCLUSIONS: Our results suggest that working with metals and pesticides could be risk factors for CVD among Hispanic/Latino workers. Further work is needed to evaluate these relationships prospectively.

PMID: 30538094

Pulmonology. 2018 Dec 6. pii: S2531-0437(18)30150-8. . [Epub ahead of print]

COPD and Cardiovascular Disease.

André S, Conde B, Fragoso E, Boléo-Tomé JP, Areias V, Cardoso J; GI DPOC-Grupo de Interesse na Doença Pulmonar Obstrutiva Crónica.

COPD is one of the major public health problems in people aged 40 years or above. It is currently the 4th leading cause of death in the world and projected to be the 3rd leading cause of death by 2020. COPD and cardiac comorbidities are frequently associated. They share common risk factors, pathophysiological processes, signs and symptoms, and act synergistically as negative prognostic factors. Cardiac disease includes a broad spectrum of entities with distinct pathophysiology, treatment and prognosis. From an epidemiological point of view, patients with COPD are particularly vulnerable to cardiac disease. Indeed, mortality due to cardiac disease in patients with moderate COPD is higher than mortality related to respiratory failure. Guidelines reinforce that the control of comorbidities in COPD has a clear benefit over the potential risk associated with the majority of the drugs utilized. On the other hand, the true survival benefits of aggressive treatment of cardiac disease and COPD in patients with both conditions have still not been clarified. Given their relevance in terms of prevalence and prognosis, we will focus in this paper on the management of COPD patients with ischemic coronary disease, heart failure and dysrhythmia.

PMID: 30527374

Nutr Hosp. 2018 Dec 3;35(6):1479-1490.

[The importance of dairy products for cardiovascular health: whole or low fat?]

[Article in Spanish; Abstract available in Spanish from the publisher]

Salas-Salvadó J, Babio N, Juárez-Iglesias M, Picó C, Ros E, Moreno Aznar LA.

The nutritional guidelines incorporate dairy products as part of a balanced and healthy diet. In almost all guidelines it is announced that dairy products have to preferably be consumed as non or low-fat version. The reason behind this recommendation is the intake of saturated fatty acids (SFA). Recently, it has been suggested that building nutritional recommendations according to the nutrient food content, leads to a limiting interpretation of the functions and properties of the consumed food. Lately, the research focus has been shifted towards the study of the food matrix, which allows assessing health effects considering all the components contained in the foods, and their impact in human health. Dairy products are the perfect example to highlight the importance of the food matrix as a determinant of the effects of nutrients on health. The potentially harmful effects of SFA on cardiometabolic health seem to be different when they are consumed within nutrient-rich foods such as yogurt, cheese or other dairy products. Epidemiological studies with large population cohorts and long term follow-up show that consumption of dairy products, especially yogurt, is not associated with an increased cardiovascular risk. Therefore, there is not enough scientific evidence to preferentially recommend the consumption of non-fat or low-fat dairy products to the general population, instead of its whole-fat version.

PMID: 30525863

Cardiovasc Diabetol. 2018 Dec 5;17(1):154.

Cognitive function in adolescence and the risk for premature diabetes and cardiovascular mortality in adulthood.

Twig G, Tirosh A, Derazne E, Haklai Z, Goldberger N, Afek A, Gerstein HC, Kark JD, Cukierman-Yaffe T

BACKGROUND: Epidemiological studies have demonstrated a relationship between cognitive function in youth and the future risk of death. Less is known regarding the relationship with diabetes related death. This study assessed the relationship between cognitive function in late adolescence and the risk for diabetes, cardiovascular- (CVD) and all-cause mortality in adulthood.

METHODS: This retrospective study linked data from 2,277,188 16-19 year olds who had general intelligence tests (GIT) conducted during pre-military recruitment assessment with cause of death as coded by the Israel Central Bureau of Statistics. The associations between cognitive function and cause-specific mortality were assessed using Cox models.

RESULTS: There were 31,268 deaths that were recorded during 41,916,603 person-years of follow-up, with a median follow-up of 19.2 (IQR 10.7, 29.5) years. 3068, 1443, 514 and 457 deaths were attributed to CVD, CHD, stroke, and diabetes, respectively. Individuals in the lowest GIT vs. highest GIT quintiles in unadjusted models had the highest risk for all-cause mortality (HR 1.84, 95% CI 1.78, 1.91), total CVD (HR 3.32, 95% CI 2.93, 3.75), CHD (HR 3.49 95% CI 2.92, 4.18), stroke (HR 3.96 95% CI 2.85, 5.5) and diabetes-related (HR 6.96 95% CI 4.68, 10.36) mortality. These HRs were attenuated following adjustment for age, sex, birth year, body-mass index, residential socioeconomic status, education and country of origin for all-cause (HR 1.23, 95% CI 1.17, 1.28), CVD (HR 1.76, 95% CI 1.52, 2.04), CHD (HR 1.7 95% CI 1.37, 2.11), stroke (HR 2.03, 95% CI 1.39, 2.98) and diabetes-related (HR 3.14 95% CI 2.00, 4.94) mortality. Results persisted in a sensitivity analyses limited to participants with unimpaired health at baseline and that accounted competing risk.

CONCLUSIONS: This analysis of over 2 million demonstrates a strong relationship between cognitive function at youth and the risk for diabetes, all-cause and CVD-related mortality independent of adolescent obesity.

BMC Endocr Disord. 2018 Dec 4;18(1):91.

Pre-diabetes and diabetes are independently associated with adverse cognitive test results: a cross-sectional, population-based study.

Dybjer E, Nilsson PM, Engström G, Helmer C, Nägga K.

BACKGROUND: Diabetes is a risk factor for cognitive impairment, but whether there is also a link between pre-diabetes and cognitive dysfunction is not yet fully established. The aim of this observational study was to investigate associations between pre-diabetes/diabetes and cognitive test results, and also between glucose levels measured during the Oral Glucose Tolerance Test (OGTT) and cognitive outcomes.
METHODS: During 2007-2012, in all 2994 people (mean age 72 years), residing in Malmö, Sweden, underwent a clinical examination including the OGTT, cardiovascular measurements including carotid-femoral pulse wave velocity (c-f PWV) and two cognitive tests, the Mini Mental State Examination (MMSE), measuring global cognitive function, and A Quick Test of Cognitive Speed (AQT), measuring processing speed and executive functioning. Regression analyses were performed to investigate associations between: (a) categories of normal or impaired glucose metabolism, and (b) OGTT measurements, respectively, as exposure variables and cognitive test results as outcomes. Adjustments were made for demographics, lifestyle factors and cardiovascular risk factors.
RESULTS: Participants with pre-diabetes and diabetes scored slightly worse cognitive test results compared to the control group. Results of participants with a long disease duration of diabetes since the baseline examination 13 years earlier were poorer (mean AQT test time 17.8 s slower than controls, $p < 0.001$). Linear associations were found between fasting and 2-h glucose and cognitive outcomes in the whole population, but also in a sub-analysis including only individuals without diabetes (for 2-h glucose and MMSE results: $B = -2.961$, $p = 0.005$). Associations were stronger for older or less physically active individuals. When adjusting for cardiovascular risk factors, most correlations were non-significant.
CONCLUSIONS: Pre-diabetes and diabetes are associated with minor deficits in global cognitive function, processing speed and executive functioning. Long-standing diabetes is associated with bigger deficits. There appears to be a continuous inverse correlation between glucose levels and cognitive test results, also for people without diabetes. Associations are stronger in older and less physically active individuals. Cardiovascular factors are important mediating factors in the pathway between diabetes and cognitive dysfunction.

PMCID: PMC6278035
PMID: 30514382

Nord J Psychiatry. 2018 Oct;72(7):455-461

Incidence of cardiovascular diseases and type-2-diabetes mellitus in patients with psychiatric disorders.

Bent-Ennakhil N, Cécile Périer M, Sobocki P, Gothefors D, Johansson G, Milea D, Empana JP.

OBJECTIVE: To assess the incidence of cardiovascular diseases (CVD) and type-2-diabetes in patients with psychiatric disorders.
METHODS: A population-based study was conducted using the Swedish national health registries. Patients were identified from the Electronic Medical Records (EMR) in 20 primary care centers and were categorized in four diagnosis cohorts according to their first psychiatric diagnosis: bipolar disorder, schizophrenia, major depressive disorder, or other mood disorder. A control cohort of patients with no psychiatric disorders followed in the same primary care centers was also identified. Incident CVD and type-2-diabetes were defined as the presence of a diagnosis of CVD or diabetes during the follow-up period in patients without prior event.
RESULTS: The age and sex standardized incidence rate of CVD was 13.5 per 1000 patient-year in the patients with any psychiatric disorder versus 6.3 per 1000 patient-year in the controls. A similar trend was observed for incident diabetes (5.7 versus 3.4 per 1000 patient-year, respectively). The bipolar disorder and the schizophrenia cohorts showed the highest standardized incidence rates.
CONCLUSION: Incidence of CVD and to a lesser extent type-2-diabetes was particularly high in patients with psychiatric disorders. This carries strong clinical implications for the prevention of CVD and type-2-diabetes in these patients.

PMID: 30513230

Clin Chem. 2019 Jan;65(1):108-118.

Determinants of Vascular Age: An Epidemiological Perspective.

Kucharska-Newton AM, Stoner L, Meyer ML.

BACKGROUND: Vascular age is an emerging health indicator and predictor of end-organ damage to the heart, brain, and kidney. Although there have been many review publications concerning risk factors for vascular aging, most include cross-sectional epidemiological studies, limiting inferences about temporality. There is a need for a review of longitudinal epidemiological studies with repeated measures of vascular structure and function to allow for a systematic examination of determinants of vascular age and the association of vascular aging with outcomes.

CONTENT: Arterial stiffness is the most frequently used measure of vascular aging. We report here results of an extensive literature review of longitudinal cohort studies with repeated measures of arterial stiffness to characterize determinants of vascular age. Additionally, we summarize population-based studies that have focused on the association of arterial stiffness with end-organ damage and adverse cardiovascular outcomes.

SUMMARY: Changes in arterial stiffness are evident in early childhood. In adults, arterial stiffness has been observed to progress at the average rate of 0.2 to 0.7 m/s for every 5 years of life. The state of the science is limited by the small number of studies with repeated measures of arterial stiffness and determinants of arterial stiffness progression, as well as limited studies in children and diverse race/ethnic groups. Several extant studies suggest that beyond age, cardiometabolic risk factors and adverse lifestyle behaviors contribute to arterial stiffening. Therefore, arterial stiffness is important in the assessment of healthy vascular aging and a possible target for the prevention of subclinical and clinical disease.

PMID: 30459170

Atherosclerosis. 2018 Nov 8;280:21-27.

Life course trajectories of cardiovascular risk: Impact on atherosclerotic and metabolic indicators.

Pollock BD, Stuchlik P, Harville EW, Mills KT, Tang W, Chen W, Bazzano LA.

BACKGROUND AND AIMS: In this analysis, we estimated population-level trajectory groups of life course cardiovascular risk to explore their impact on mid-life atherosclerotic and metabolic outcomes.
METHODS: This prospective study followed n = 1269 Bogalusa Heart participants, each with at least 4 study visits from childhood in 1973 through adulthood in 2016. We used discrete mixture modeling to determine trajectories of cardiovascular risk percentiles from childhood to adulthood. Outcomes included mid-life subclinical atherosclerotic measures [(carotid intima-media thickness (cIMT), pulse wave velocity (PWV)], metabolic indicators [(diabetes and body mass index (BMI)], and short physical performance battery (SPPB).
RESULTS: Between the mean ages of 9.6-48.3 years, we estimated five distinct trajectory groups of life course cardiovascular risk (High-Low, High-High, Mid-Low, Low-Low, and Low-High). Adult metabolic and vascular outcomes were significantly determined by life course cardiovascular risk trajectory groups (all $p < 0.01$). Those in the High-Low group had lower risks of diabetes (20% vs. 28%, respectively; $p = .12$) and lower BMIs (32.4 kg/m2vs. 34.6 kg/m2; $p = .06$) than those who remained at high risk (High-High) throughout life. However, the High-Low group had better cIMT (0.89 mm vs. 1.05 mm; $p < .0001$) and PWV (7.8 m/s vs. 8.2 m/s; $p = .03$) than the High-High group. For all outcomes, those in the Low-Low group fared best.
CONCLUSIONS: We found considerable movement between low- and high-relative cardiovascular risk strata over the life course. Children who improved their relative cardiovascular risk over the life course achieved better mid-life atherosclerotic health despite maintaining relatively poor metabolic health through adulthood.

PMID: 30453117

Atherosclerosis. 2018 Nov 8;280:1-6.

Incidence of cardiovascular disease in familial combined hyperlipidemia: A 15-year follow-up study.

Luijten J, van Greevenbroek MMJ, Schaper NC, Meex SJR, van der Steen C, Meijer LJ, de Boer D, de Graaf J, Stehouwer CDA, Brouwers MCGJ.

BACKGROUND AND AIMS: Familial combined hyperlipidemia (FCHL) is a complex dyslipidemia associated with premature cardiovascular disease (CVD). The present study was conducted to 1) determine the incidence of CVD in FCHL in this era of protocolled, primary prevention; and 2) examine whether cardiovascular risk estimation based on the Systemic Coronary Risk Estimation (SCORE) chart, as proposed in the 2016 ESC/EAS guidelines for the management of dyslipidemia, is justified in FCHL.
METHODS: FCHL patients, their normolipidemic (NL) relatives and spouses originally included in our baseline cohort in 1998-2005 (n = 596) were invited for a follow-up visit to determine the incidence of CVD, defined as (non-)fatal coronary artery disease, ischemic stroke and peripheral artery disease requiring invasive treatment.
RESULTS: Follow-up data (median: 15 years) was acquired for 85% of the original cohort. The cumulative incidence of CVD was significantly higher in FCHL patients than in spouses (23.6% versus 4.7%; hazard ratio (HR): 5.4, 95%CI: 2.0-14.6; HR after adjustment for risk factors included in SCORE: 4.7, 95%CI: 1.6-13.8), but not in NL relatives compared to spouses (5.8% versus 4.7%). The SCORE chart tended to overestimate CVD risk in the spouses (observed [O]/expected [E] ratio:0.2, p = 0.01), but not in FCHL patients (O/E:1.3, p = 0.50).
CONCLUSIONS: Risk of primary CVD is still substantially increased in FCHL patients, despite preventive measures. The overestimation of CVD risk by the SCORE chart - a nowadays frequently observed phenomenon thanks to improved primary prevention - was not seen in FCHL. These results suggest that more aggressive treatment is justified to avoid excessive CVD in FCHL.

PMID: 30448567

Rev Clin Esp. 2018 Nov 15. pii: S0014-2565(18)30281-9 [Epub ahead of print]

Analysis of hospitalizations by cardiovascular disease in the population with diabetes in Spain.

Zapatero-Gaviria A, Gómez-Huelgas R, Canora-Lebrato J, Ena-Muñoz J, Romero-Sánchez M, Mendez-Bailón M, Marco-Martínez J, Barba-Martín R.

OBJECTIVES: Diabetes mellitus is associated with a marked increase in cardiovascular disease. In this study, we analysed the prevalence of diabetes mellitus in hospitalised patients in Spain in 2015 and the burden of associated cardiovascular disease.
METHODS: By analysing the 2015 minimum basic data set (MBDS) of the Spanish Ministry of Health, we included all patients discharged with a diagnosis of diabetes mellitus. We describe the epidemiological characteristics, distribution by the various hospital departments and the presence of cardiovascular disease.
RESULTS: In 2015, there was 3,727,583 hospital discharges in Spain, 619,188 of which involved patients with diabetes (16.7%), 56.8% of whom were men and with a mean age of 73.2years. The prevalence of cardiovascular disease was 40.8%, distributed among congestive heart failure (20.1%), cerebrovascular disease (10.3%), coronary artery disease (9.4%) and peripheral arterial disease (9.1%). Most of the patients were admitted to internal medicine (34.2%), cardiology (9.5%) and general surgery (8.9%) departments. The mean overall stay was 8.2days, the readmission rate at 30days was 14%, and the mortality rate was 6.8%. The patients hospitalized in internal medicine had higher severity levels (3-4) than those hospitalized in other medical departments (41.9% vs. 31.6%, respectively; P<.01) and those hospitalized in surgical departments (11.2%; P<.01).
CONCLUSIONS: Diabetes mellitus is a significant comorbidity for patients hospitalized in internal medicine. A significant proportion of these patients present cardiovascular disease, mostly heart failure.

PMID: 30447849

Int J Epidemiol. 2018 Dec 1;47(6):1830-1845.

Lipid metabolic networks, Mediterranean diet and cardiovascular disease in the PREDIMED trial.

Wang DD, Zheng Y, Toledo E, Razquin C, Ruiz-Canela M, Guasch-Ferré M, Yu E, Corella D, Gómez-Gracia E, Fiol M, Estruch R, Ros E, Lapetra J, Fito M, Aros F, Serra-Majem L, Clish CB, Salas-Salvadó J, Liang L, Martínez-González MA, Hu FB.

Background: Perturbed lipid metabolic pathways may play important roles in the development of cardiovascular disease (CVD). However, existing epidemiological studies have focused more on discovering individual lipid metabolites for CVD risk prediction rather than assessing metabolic pathways.
Methods: This study included a subcohort of 787 participants and all 230 incident CVD cases from the PREDIMED trial. Applying a network-based analytical method, we identified lipid subnetworks and clusters from a global network of 200 lipid metabolites and linked these subnetworks/clusters to CVD risk.
Results: Lipid metabolites with more double bonds clustered within one subnetwork, whereas lipid metabolites with fewer double bonds clustered within other subnetworks. We identified 10 lipid clusters that were divergently associated with CVD risk. The hazard ratios [HRs, 95% confidence interval (CI)] of CVD per a 1-standard deviation (SD) increment in cluster score were 1.39 (1.17-1.66) for the hydroxylated phosphatidylcholine (HPC) cluster and 1.24 (1.11-1.37) for a cluster that included diglycerides and a monoglyceride with stearic acyl chain. Every 1-SD increase in the score of cluster that included highly unsaturated phospholipids and cholesterol esters was associated with an HR for CVD of 0.81 (95% CI, 0.67-0.98). Despite a suggestion that MedDiet modified the association between a subnetwork that included most lipids with a high degree of unsaturation and CVD, changes in lipid subnetworks/clusters during the first-year follow-up were not significantly different between intervention groups.
Conclusions: The degree of unsaturation was a major determinant of the architecture of lipid metabolic network. Lipid clusters that strongly predicted CVD risk, such as the HPC cluster, warrant further functional investigations.

PMCID: PMC6280948 [Available on 2019-12-01]
PMID: 30428039

Diabetes. 2019 Feb;68(2):409-419. Epub 2018 Nov 8.

Risk Factor Modeling for Cardiovascular Disease in Type 1 Diabetes in the Pittsburgh Epidemiology of Diabetes Complications (EDC) Study: A Comparison With the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications Study (DCCT/EDIC).

Miller RG, Costacou T, Orchard TJ.

In a recent Diabetes Control and Complications Trial (DCCT)/Epidemiology of Diabetes Interventions and Complications (EDIC) study report, mean HbA1c was the strongest predictor of cardiovascular disease (CVD) after age. In DCCT/EDIC, mean diabetes duration was 6 years (median 4) at baseline and those with high blood pressure or cholesterol were excluded. We now replicate these analyses in the Pittsburgh Epidemiology of Diabetes Complications (EDC) prospective cohort study of childhood-onset (at <17 years of age) type 1 diabetes, with similar age (mean 27 years in both studies) but longer diabetes duration (mean 19 years and median 18 years) and no CVD risk factor exclusion at baseline. CVD incidence (CVD death, myocardial infarction (MI), stroke, revascularization, angina, or ischemic electrocardiogram) was associated with diabetes duration, most recent albumin excretion rate (AER), updated mean triglycerides, baseline hypertension, baseline LDL cholesterol, and most recent HbA1c Major atherosclerotic cardiovascular events (CVD death, MI, or stroke) were associated with diabetes duration, most recent AER, baseline systolic blood pressure, baseline smoking, and updated mean HbA1c Compared with findings in DCCT/EDIC, traditional risk factors similarly predicted CVD; however AER predominates in EDC and HbA1c in DCCT/EDIC. Thus, the relative impact of HbA1c and kidney disease in type 1 diabetes varies according to diabetes duration.

PMID: 30409781

J Renin Angiotensin Aldosterone Syst. 2018 Oct-Dec;19(4):

Salt and cardiovascular disease in PURE: A large sample size cannot make up for erroneous estimations.

Tan M, He FJ, MacGregor GA.

The latest Prospective Urban Rural Epidemiology (PURE) study claims that salt reduction should be confined to settings where its intake exceeds 12.7 g/day and that eating less than 11.1 g/day of salt could increase cardiovascular risk. More specifically, Mente et al. suggested that (a) salt intake was positively associated with stroke only when it exceeded 12.7 g/day, (b) salt intake was inversely associated with myocardial infarction and total mortality, and (c) these associations were largely independent of blood pressure. These provocative findings challenge the robust evidence on the role of salt reduction in the prevention of cardiovascular disease and call into question the World Health Organization's global recommendation to reduce salt intake to less than 5 g/day. However, Mente et al.'s re-analysis of the PURE data has several severe methodological problems, including erroneous estimations of salt intake from a single spot urine using the problematic Kawasaki formula. As such, these implausible results cannot be used to refute the strong evidence supporting the benefits of salt reduction for the general population worldwide.

PMCID: PMC6240978
PMID: 30404579 [Indexed for MEDLINE]

Metabolism. 2018 Nov 3. pii: S0026-0495(18)30229-4.

Obesity and cardiovascular disease: revisiting an old relationship.

Koliaki C, Liatis S, Kokkinos A.

A wealth of clinical and epidemiological evidence has linked obesity to a broad spectrum of cardiovascular diseases (CVD) including coronary heart disease, heart failure, hypertension, stroke, atrial fibrillation and sudden cardiac death. Obesity can increase CVD morbidity and mortality directly and indirectly. Direct effects are mediated by obesity-induced structural and functional adaptations of the cardiovascular system to accommodate excess body weight, as well as by adipokine effects on inflammation and vascular homeostasis. Indirect effects are mediated by co-existing CVD risk factors such as insulin resistance, hyperglycemia, hypertension and dyslipidemia. Adipose tissue (AT) quality and functionality are more relevant aspects for cardiometabolic risk than its total amount. The consequences of maladaptive AT expansion in obesity are local and systemic: the local include inflammation, hypoxia, dysregulated adipokine secretion and impaired mitochondrial function; the systemic comprise insulin resistance, abnormal glucose/lipid metabolism, hypertension, a pro-inflammatory and pro-thrombotic state and endothelial dysfunction, all of which provide linking mechanisms for the association between obesity and CVD. The present narrative review summarizes the major pathophysiological links between obesity and CVD (traditional and novel concepts), analyses the heterogeneity of obesity-related cardiometabolic consequences, and provides an overview of the cardiovascular impact of weight loss interventions.

PMID: 30399375

Curr Hypertens Rep. 2018 Oct 25;20(12):102.

The Relationship Between Psychosocial Status and Hypertensive Condition.

Matei Ș, Cutler SJ, Preda M, Dorobanțu M, Ilinca C, Gheorghe-Fronea O, Rădulescu L, Oprescu N, Deaconu A, Zorilă C, Dorobanțu B.

PURPOSE OF REVIEW: The aim of the paper is to test the influence of social status and psychological well-being (independent variables) on hypertensive condition (dependent variable), when adjusting for traditional risk factors of cardiovascular disease (control variables). The analysis is based on data collected from SEPHAR III, a nationally representative epidemiologic study of the Romanian adult population.
RECENT FINDINGS: Understanding the social roots of health issues is of considerable importance in developing effective strategies and policies. In this context, most studies explain the influence of social and psychological indicators on hypertension by considering the mediating effects of class-based lifestyle practices, i.e., the full range of economic, social, or symbolic resources available to particular social classes. However, the effect of traditional risk factors of cardiovascular disease in shaping the relationship between psychosocial status and hypertension has remained mostly unexplored. The influence of socioeconomic status and psychological well-being on hypertensive condition is assimilated by age as a variable with both biological and social foundations. Age appears not only as a risk factor for high blood pressure but also as an emergent component of psychosocial status. Furthermore, people without higher education are more likely to be known hypertensives with uncontrolled blood pressure values. Social and economic vulnerabilities (e.g., age, education) are interrelated with several health conditions, which support the necessity to develop and implement integrated public policies based on interventions coordinated across several domains. Moreover, social and psychological determinants that predipose to certain health risks should be considered in medical practice.

PMID: 30361797

Molecules. 2018 Oct 23;23(11). pii: E2730.

Current Therapies Focused on High-Density Lipoproteins Associated with Cardiovascular Disease.

Estrada-Luna D, Ortiz-Rodriguez MA, Medina-Briseño L, Carreón-Torres E, Izquierdo-Vega JA, Sharma A, Cancino-Díaz JC, Pérez-Méndez O, Belefant-Miller H, Betanzos-Cabrera G.

High-density lipoproteins (HDL) comprise a heterogeneous family of lipoprotein particles divided into subclasses that are determined by density, size and surface charge as well as protein composition. Epidemiological studies have suggested an inverse correlation between High-density lipoprotein-cholesterol (HDL-C) levels and the risk of cardiovascular diseases and atherosclerosis. HDLs promote reverse cholesterol transport (RCT) and have several atheroprotective functions such as anti-inflammation, anti-thrombosis, and anti-oxidation. HDLs are considered to be atheroprotective because they are associated in serum with paraoxonases (PONs) which protect HDL from oxidation. Polyphenol consumption reduces the risk of chronic diseases in humans. Polyphenols increase the binding of HDL to PON1, increasing the catalytic activity of PON1. This review summarizes the evidence currently available regarding pharmacological and alternative treatments aimed at improving the functionality of HDL-C. Information on the effectiveness of the treatments has contributed to the understanding of the molecular mechanisms that regulate plasma levels of HDL-C, thereby promoting the development of more effective treatment of cardiovascular diseases. For that purpose, Scopus and Medline databases were searched to identify the publications investigating the impact of current therapies focused on high-density lipoproteins.

PMCID: PMC6278283
PMID: 30360466 [Indexed for MEDLINE]

Endocr Rev. 2018 Oct 11. [Epub ahead of print]

The Forgotten Lipids: Triglycerides, Remnant Cholesterol, and Atherosclerotic Cardiovascular Disease Risk.

Sandesara PB, Virani SS, Fazio S, Shapiro MD.

Atherosclerotic cardiovascular disease (ASCVD) remains the leading cause of death worldwide. Low-density lipoprotein cholesterol (LDL-C) is a well-established mediator of atherosclerosis and a key target for intervention for the primary and secondary prevention of ASCVD. However, despite significant reduction in LDL-C, patients continue to have recurrent ASCVD events. Hypertriglyceridemia maybe an important contributor of this residual risk. Observational and genetic epidemiological data strongly support a causal role of triglycerides and the cholesterol content within triglyceride-rich lipoproteins (TGRL) and/or remnant cholesterol (RC) in the development of ASCVD. TGRL are comprised of hepatically derived very low-density lipoprotein (VLDL) and intestinally derived chylomicrons. RC is the cholesterol content of all TGRL and plasma triglycerides serve as a surrogate measure of TGRL and RC. Although lifestyle modification remains the cornerstone for management of hypertriglyceridemia, many novel drugs are in development and have shown impressive TG lowering efficacy. Several ongoing randomized controlled trials are under way to examine the impact of these novel agents on ASCVD outcomes. In this comprehensive review, we provide an overview of the biology, epidemiology and genetics of triglycerides and ASCVD and discuss current and novel triglyceride lowering therapies under development.

PMID: 30312399

Curr Cardiol Rep. 2018 Oct 11;20(12):125

Diabetic Dyslipidemia: Epidemiology and Prevention of Cardiovascular Disease and Implications of Newer Therapies.

Warraich HJ, Rana JS.

PURPOSE OF REVIEW: Dyslipidemia in patients with T2DM confers significant additional risk of adverse outcomes to patients with cardiovascular disease (CVD). These patients carry residual risk of adverse outcomes despite optimal management with conventional therapy such as lifestyle changes and statin therapy. The role of both nonstatin monotherapy in statin-intolerant patients and combination therapy with statins in patients with high risk of CVD events has been well studied. We sought to review the role of newer therapies in risk reduction in these patients.
RECENT FINDINGS: Traditionally, non-statin options have included medications such as niacin, ezetimibe, fenofibrate, and n-3 fatty acids. Recently, drugs such as ezetimibe, inclisiran, and PCSK9 inhibitors have been studied with favorable results without an increased risk of developing new-onset diabetes. These medications hold the promise of increasing options to reduce cardiovascular risk in patients with T2DM. The role of newer non-statin therapies in patients with diabetic dyslipidemia in combination with statins needs to be further explored.

PMID: 30311078

Am J Cardiol. 2018 Dec 15;122(12):2157-2165.

Acute and Subacute Triggers of Cardiovascular Events.

Schwartz BG, Kloner RA, Naghavi M.

Inability to predict short-term cardiovascular (CV) events and take immediate preemptive actions has long been the Achilles heel of cardiology. However, certain triggers of these events have come to light. Although these triggers are nonspecific and are part of normal life, studying their temporal relationship with the onset of CV events provides an opportunity to alert high-risk atherosclerotic patients who may be most vulnerable to such triggers, the "vulnerable patient". Herein, we review the literature and shed light on the epidemiology and underlying pathophysiology of different triggers. We describe that certain adrenergic triggers can precipitate a CV event within minutes or hours; whereas triggers that elicit an immune or inflammatory response such as infections may tip an asymptomatic "vulnerable patient" to become symptomatic days and weeks later. In conclusion, healthcare providers should counsel high-risk CV patients (e.g., in secondary prevention clinics or those with coronary artery Calcium >75th percentile) on the topic, advise them to avoid such triggers, take protective measures once exposed, and seek emergency care immediately after becoming symptomatic after such triggers. Furthermore, clinical trials targeting triggers (prevention or intervention) are needed.

PMID: 30309628

Angiology. 2018 Oct 9:3319718799967. [Epub ahead of print]

Perirenal Fat: A Unique Fat Pad and Potential Target for Cardiovascular Disease.

Liu BX, Sun W, Kong XQ.

Although visceral obesity is recognized as a risk factor for cardiovascular diseases (CVDs), the efficacy of omental fat removal in CVD treatment is still controversial. There is a need to identify other visceral fat depots for CVD management. This review aims to provide a summary on perirenal fat as an important risk factor for CVD. Studies on epidemiology, anatomy, and function of perirenal fat were reviewed. Observational studies in humans suggest that excessive perirenal fat increases the risk of hypertension and coronary heart disease. Anatomy studies prove that perirenal fat is unique compared to other connective tissues in that it is well vascularized, innervated, and drains into the lymphatic system. Other special morphological features include a complete fascia border, sympathetic-independent development of architecture, and proximity to the kidneys. Based on these anatomical features, perirenal fat regulates the cardiovascular system presumably via neural reflex, adipokine secretion, and fat-kidney interaction. These new insights suggest that perirenal fat may constitute a promising target for CVD management.

PMID: 30301366

Front Med. 2018 Dec;12(6):658-666.

Epidemic obesity in children and adolescents: risk factors and prevention.

Lee EY, Yoon KH.

The prevalence of obesity among children and adolescents (aged 2-18 years) has increased rapidly, with more than 100 million affected in 2015. Moreover, the epidemic of obesity in this population has been an important public health problem in developed and developing countries for the following reasons. Childhood and adolescent obesity tracks adulthood obesity and has been implicated in many chronic diseases, including type 2 diabetes, hypertension, and cardiovascular disease. Furthermore, childhood and adolescent obesity is linked to adulthood mortality and premature death. Although an imbalance between caloric intake and physical activity is a principal cause of childhood and adolescent obesity, environmental factors are exclusively important for development of obesity among children and adolescents. In addition to genetic and biological factors, socioenvironmental factors, including family, school, community, and national policies, can play a crucial role. The complexity of risk factors for developing obesity among children and adolescents leads to difficulty in treatment for this population. Many interventional trials for childhood and adolescent obesity have been proven ineffective. Therefore, early identification and prevention is the key to control the global epidemic of obesity. Given that the proportion of overweight children and adolescents is far greater than that of obesity, an effective prevention strategy is to focus on overweight youth, who are at high risk for developing obesity. Multifaceted, comprehensive strategies involving behavioral, psychological, and environmental risk factors must also be developed to prevent obesity among children and adolescents.

PMID: 30280308

Atherosclerosis. 2018 Oct;277:289-297.

Epidemiology of familial hypercholesterolaemia: Community and clinical.

Vallejo-Vaz AJ, Ray KK.

Familial hypercholesterolaemia (FH) is a genetic disorder affecting the metabolism of low-density lipoprotein (LDL) particles, leading to high LDL-cholesterol levels maintained over time and higher risk of cardiovascular disease (CVD) early in life. Contemporary studies have challenged prior estimations of FH prevalence and suggest this condition to be more frequent than previously considered, with an overall prevalence rate of 1:200-300 individuals in the general population (1:160,000-300,000 for homozygous FH). However, prevalence of FH varies around the world. In part this is due to an artefact of approaches of detection and methods used to diagnose FH (e.g. lack of gold standard for diagnosis of FH, different criteria applied, availability of genetic testing). But also due to intrinsic characteristic of different populations, e.g. higher presence of founder effects or rates of consanguinity. Additionally, results from many regions are lacking and it is estimated that only a small percentage of subjects with FH would have been diagnosed overall. FH entails a significantly higher risk of CVD, reported to be higher than that estimated by conventional risk assessment tools for the general population. This risk is mainly driven by coronary heart disease. Despite this evidence, low rates of patients meet therapeutic targets for cardiovascular prevention, and implementation of therapy (high intensity statins, combination therapy) is needed. The introduction of novel lipid-lowering therapies may improve this situation. In the present review, we discuss the epidemiology of FH overall, with special attention to different aspects related to prevalence, cardiovascular risk and prognosis, and treatment of FH.

PMID: 30270061

Liver Int. 2019 Jan;39(1):197-204.

Cardiovascular risk factors in non-alcoholic fatty liver disease.

Hagström H, Nasr P, Ekstedt M, Hammar U, Stål P, Askling J, Hultcrantz R, Kechagias S.

BACKGROUND & AIMS: Patients with non-alcoholic fatty liver disease (NAFLD) are at an increased risk for cardiovascular disease (CVD). It is unclear whether histological variables may help predict CVD risk. We evaluated histology and traditional CV risk factors as predictors of CVD outcomes in a large NAFLD cohort.
METHODS: We included 603 biopsy-proven NAFLD patients free of baseline CVD and matched these (1:10, by age, sex and municipality) to 6269 population controls. All individuals were cross-linked to national registries to ascertain incident CVD events, defined as acute ischaemic heart disease or stroke. The presence of CV risk factors and liver histology were available in NAFLD patients only. Cox regression models were used to estimate hazard ratios (HR) for incident CVD.
RESULTS: During a mean follow-up of 18.6 years, 168 (28%) of NAFLD patients and 1325 (21%) of controls experienced a CVD event (HR 1.54, 95%CI 1.30-1.83). Within the NAFLD cohort, age, male sex, type 2 diabetes, smoking and triglycerides were associated with risk of CVD. Taking these CV risk factors into account, no histological parameter, including presence of NASH and fibrosis stage, were associated with incident CVD.
CONCLUSIONS: Patients with NAFLD are at an increased risk for CVD compared to matched controls, but histological parameters do not seem to independently predict this risk.

PMID: 30253056

Atherosclerosis. 2018 Nov;278:1-6 Epub 2018 Sep 8.

Prediabetes and cardiovascular disease risk: A nested case-control study.

Hu H, Mizoue T, Sasaki N, Ogasawara T, Tomita K, Nagahama S, Hori A, Nishihara A, Imai T, Yamamoto M, Eguchi M, Kochi T, Miyamoto T, Honda T, Nakagawa T, Yamamoto S, Okazaki H, Uehara A, Shimizu M, Murakami T, Kuwahara K, Nanri A, Konishi M Kabe I Dohi S; Japan Epidemiology Collaboration on Occupational Health Study Group.

BACKGROUND AND AIMS: We aimed to examine the risk of cardiovascular disease (CVD) with persistent prediabetes during the last four years prior to a CVD event in a large occupational cohort in Japan.
METHODS: We performed a nested case-control study using data from the Japan Epidemiology Collaboration on Occupational Health Study. A total of 197 registered cases of CVD were identified and matched individually with 985 controls according to age, sex, and worksite. Prediabetes was defined as fasting plasma glucose 100-125 mg/dL and/or HbA1c 5.7-6.4%. Persistent prediabetes was defined as having prediabetes at years one and four prior to the onset/index date; persistent normoglycemia was similarly defined. Associations between prediabetes and CVD risk were assessed using conditional logistic regression models.
RESULTS: Compared with people with persistent normoglycemia over the four years prior to the onset/index date, the unadjusted odds ratio (95% confidence interval) for CVD was 2.88 (1.56, 5.32) for people with persistent prediabetes. After adjusting for BMI, smoking, hypertension, and dyslipidemia assessed four years before the onset/index date, the association was slightly attenuated to an OR (95% confidence interval) of 2.62 (1.31, 5.25). Prediabetes assessed at single time points was also associated with an elevated risk of CVD, with multivariable-adjusted odds ratio (95% confidence interval) of 1.72 (1.12, 2.64) and 2.13 (1.32, 3.43) for prediabetes at one and four years prior to the onset/index date, respectively.
CONCLUSIONS: Prediabetes is associated with an increased risk of CVD. Identification and management of prediabetes are important for the prevention of CVD.

PMID: 30227266

Sci Total Environ. 2018 Dec 1;643:1041-1053.

Air pollution: A public health approach for Portugal.

Torres P, Ferreira J, Monteiro A, Costa S, Pereira MC, Madureira J, Mendes A, Teixeira JP.

At the global level, several epidemiological studies have conclusively pointed out the associations between short-term exposure to air pollution and acute health effects, and long-term exposure with adverse health effects such as premature mortality from severe respiratory and cardiovascular diseases. This study intended to characterize exposures and their adverse health effects. Three independent sets of vectors were analyzed on a nationwide level and annual basis: air pollutant emissions, ambient air concentrations and health indicators of the period 2009 to 2015. The emissions analysis, for the studied pollutants, pointed out the main findings: (i) Lisbon Metropolitan Area presents the most problematic region with regard to the emissions of all the pollutants under study; (ii) the regions of the Alentejo and Algarve showed reduced emissions of the studied pollutants compared to other parts of the country; (iii) Northern regions PM10 concentrations decreased during the two years in analysis. Regarding the analysis of air quality, it was concluded that: (i) regarding ozone, concentration shown a decreasing trend throughout the country; (ii) nitrogen dioxide and particulate matter, concentrations demonstrated an increasing trend in most of the northern part of the country; (iii) the regions of Alentejo and Lisbon Metropolitan Area showed increasing trends for sulfur dioxide and fine particles for the evaluated period. Decreasing trends in mortality associated with cardiovascular and respiratory causes are found mainly in the Alentejo and Algarve regions. In comparison, the North, Central regions, as well as, Lisbon Metropolitan Area exhibited higher mortality values related to this health indicators.

PMID: 30189521

Nutr Metab Cardiovasc Dis. 2018 Oct;28(10):1036-1044.

Incidence of type 2 diabetes, hypertension, and dyslipidemia in metabolically healthy obese and non-obese.

Fingeret M, Marques-Vidal P, Vollenweider P.

BACKGROUND AND AIMS: Metabolically healthy obese (MHO) individuals are devoid of many metabolic abnormalities, but how this condition is maintained over time remains debated. We assessed the prevalence of MHO over time and the incidence of hypertension (HTN), dyslipidemia, and type 2 diabetes mellitus (T2DM) in MHO as compared with metabolically healthy non obese (MHNO).
METHODS AND RESULTS: Prospective, population-based study including 3038 participants (49.9 ± 9.9 years; 1753 women) free from metabolic syndrome and cardiovascular disease at baseline and examined after a follow-up of 5.6 years and 10.9 years on average. At each follow-up, prevalence of MHO, MHNO, metabolically unhealthy not obese (MUNO), and metabolically unhealthy obese (MUO), as well as of HTN, dyslipidemia, and T2DM, was calculated and stratified by sex, age group, and education. At baseline, 179 (5.7%) MHO participants were identified, of which 62 (34.6%) and 79 (44.1%) remained MHO at 5.6 and 10.9 years follow-up, respectively. At 5.6 years follow-up, MHO participants were more likely to develop low HDL or be on hypolipidemic medication [multivariable-adjusted OR (95% CI): 1.56 (1.02-2.38)], to have dyslipidemia [1.94 (1.33-2.82)], and high triglycerides [2.07 (1.36-3.14)] than MHNO. At 10.9 years follow-up, MHO participants were significantly more likely to develop T2DM [3.44 (1.84-6.43)], dyslipidemia [1.64 (1.14-2.38)], and low HDL or be prescribed hypolipidemic medication [1.57 (1.08-2.27)] than MHNO. Conversely, no differences were found regarding hypertension.
CONCLUSION: A considerable fraction of MHO individuals lose their status over time, and in metabolically healthy adults, obesity confers a higher risk of developing cardiovascular risk factors.

PMID: 30139688

Eur J Prev Cardiol. 2018 Nov;25(17):1799-1810. Epub 2018 Aug 1.

What constitutes the 'Minimal Care' interventions of the nurse, physiotherapist, dietician and psychologist in Cardiovascular Rehabilitation and secondary prevention: A position paper from the Italian Association for Cardiovascular Prevention, Rehabilitation and Epidemiology.

Fattirolli F, Bettinardi O, Angelino E, da Vico L, Ferrari M, Pierobon A, Temporelli D, Agostini S, Ambrosetti M, Biffi B, Borghi S, Brazzo S, Faggiano P, Iannucci M, Maffezzoni B, Masini ML, Mazza A, Pedretti R, Sommaruga M, Barro S, Griffo R, Piepoli M.

BACKGROUND: In cardiovascular prevention and rehabilitation, care activities are carried out by different professionals in coordination, each with their own specific competence. This GICR-IACPR position paper has analysed the interventions performed by the nurse, physiotherapist, dietician and psychologist in order to identify what constitutes minimal care, and it lists the activities that are fundamental and indispensable for each team member to perform in clinical practice.

RESULTS: In analysing each type of intervention, the following dimensions were considered: the level of clinical care complexity, determined both by the disease and by environmental factors; the 'area' complexity, i.e. the specific level of competence required of the professional in each professional section; organisational factors, i.e. whether the care is performed in an inpatient or outpatient setting; duration of the rehabilitation intervention. The specific contents of minimal care have been identified for each professional area together with the specific goals, the assessment tools and the main essential interventions. For the assessments, only a few validated tools have been indicated, leaving the choice of which instrument to use to the individual professional based on experience and usual practice.

CONCLUSION: For the interventions, attention has been focused on conditions of major complexity requiring special care, taking into account the different care settings, the clinical conditions secondary to the disease event, and the distinct tasks of each area according to the operator's specific role. The final report performed by each professional has also been included.

PMID: 30066589

Eur J Intern Med. 2018 Nov;57:1-6.

Cardiovascular disease risk unmasked by pregnancy complications.

Jasper R, Skelding K.

Pregnancy related complications indicate a propensity for atherosclerotic disease. Epidemiologic data demonstrate early onset cardiovascular disease in women with a history of pregnancy loss, preterm pregnancy or pregnancy complicated by intrauterine growth restriction. Early onset diabetes, increased rates of MI and increased rates of stroke are more prevalent after gestational diabetes. In addition, hypertensive disorders of pregnancy mark significant pathophysiologic changes, including vascular dysfunction and immunologic changes, which induce atherogenesis and result in a substantial increase in rates of stroke, ischemic heart disease and cardiac mortality. Metabolic, endothelial and inflammatory changes are responsible for either the early onset or early recognition of cardiovascular disease propensity in patients who experience a complicated pregnancy. Therefore, the American Heart Association guidelines recognize pregnancy related complications as an independent risk factor for heart disease. This review informs physicians of epidemiologic data and, guideline recommendations and is meant to guide physicians in early interventions including provider education, routine post-partum multidisciplinary (primary care, obstetrics, cardiology) evaluation, risk factor monitoring and control after a complicated pregnancy.

PMID: 30055847

J Cell Physiol. 2018 Nov;233(11):8508-8525.

Serum C-reactive protein in the prediction of cardiovascular diseases: Overview of the latest clinical studies and public health practice.

Avan A, Tavakoly Sany SB, Ghayour-Mobarhan M, Rahimi HR, Tajfard M, Ferns G.

Cardiovascular disease is the most common cause of morbidity and mortality globally. Epidemiological studies using high-sensitivity assays for serum C-reactive protein have shown a consistent association between cardiovascular disease risk and serum C-reactive protein concentrations. C-reactive protein is a biomarker for inflammation, and has been established in clinical practice as an independent risk factor for cardiovascular disease events. There is evidence that serum C-reactive protein is an excellent biomarker of cardiovascular disease and is also an independent and strong predictor of adverse cardiovascular events. Further characterization of the impact and influence of lifestyle exposures and genetic variation on the C-reactive protein response to cardiovascular disease events may have implications for the therapeutic approaches to reduce cardiovascular disease events. This review summarizes the studies that have examined the association between serum C-reactive protein and the risk of cardiovascular disease. We also discuss the impact of independent factors and C-reactive protein genetic polymorphisms on baseline plasma C-reactive protein levels.

PMID: 29932219

Immunol Invest. 2018 Oct;47(7):689-699.

Interleukin-6 as a Predictor of the Risk of Cardiovascular Disease: A Meta-Analysis of Prospective Epidemiological Studies.

Zhang B, Li XL, Zhao CR, Pan CL, Zhang Z.

OBJECTIVE: The etiology of cardiovascular disease (CVD) is complex owing to the interactions of genetic variance with environmental factors. Inflammatory processes are now being increasingly implicated in the pathogenesis of CVD. This meta-analysis investigated the potential role of interleukin-6 (IL-6) as a risk factor for CVD development in healthy individuals.
METHODS: Literature search was carried out in multiple electronic databases, and study selection followed a priori eligibility criteria. Meta-analyses of standardized mean differences were carried out to determine an overall effect size of the difference in IL-6 levels between CVD cases and non-CVD matched controls. Meta-regression analyses were performed to examine the relationship between the IL-6 levels in CVD cases and several explanatory variables.
RESULTS: Seventeen studies enrolling 288738 healthy individuals with an average follow-up duration of 7.4 ± 4.1 years were found eligible. Overall, data of 5400 CVD cases and 14607 matched non-CVD controls are used in the present meta-analysis. Baseline IL-6 levels were significantly higher in CVD cases than in non-CVD controls (standardized mean difference [95% confidence interval]) of 0.14 [0.09, 0.20]/mean difference of 0.36 [0.28, 0.44] picogram per milliliter). Total cholesterol, LDL-cholesterol, and triglyceride levels were also significantly higher, and HDL-cholesterol levels were significantly lower in CVD cases in comparison with the controls. Systolic blood pressure and total cholesterol levels had a significantly positive relationship, whereas triglyceride levels had a significantly inverse relationship with the levels of IL-6.
CONCLUSION: Higher IL-6 levels in healthy individuals are associated with CVD risk, which is co-associated with hypertension and hypercholesterolemia.

PMID: 29873573 [Indexed for MEDLINE]

Am J Epidemiol. 2018 Oct 1;187(10):2126-2135..

Associations of Biomarker-Calibrated Intake of Total Sugars With the Risk of Type 2 Diabetes and Cardiovascular Disease in the Women's Health Initiative Observational Study.

Tasevska N, Pettinger M, Kipnis V, Midthune D, Tinker LF, Potischman N, Neuhouser ML, Beasley JM, Van Horn L, Howard BV, Liu S, Manson JE, Shikany JM, Thomson CA, Prentice RL.

The inconsistent findings from epidemiologic studies relating total sugars (TS) consumption to cardiovascular disease (CVD) or type 2 diabetes (T2D) risk may be partly due to measurement error in self-reported intake. Using regression calibration equations developed based on the predictive biomarker for TS and recovery biomarker for energy, we examined the association of TS with T2D and CVD risk, before and after dietary calibration, in 82,254 postmenopausal women participating in the Women's Health Initiative Observational Study. After up to 16 years of follow-up (1993-2010), 6,621 T2D and 5,802 CVD incident cases were identified. The hazard ratio for T2D per 20% increase in calibrated TS was 0.94 (95% confidence interval (CI): 0.77, 1.15) in multivariable energy substitution, and 1.00 (95% CI: 0.85, 1.18) in energy partition models. Multivariable hazard ratios for total CVD were 0.97 (95% CI: 0.87, 1.09) from energy substitution, and 0.91 (95% CI: 0.80, 1.04) from energy partition models. Uncalibrated TS generated a statistically significant inverse association with T2D and total CVD risk in multivariable energy substitution and energy partition models. The lack of conclusive findings from our calibrated analyses may be due to the low explanatory power of the calibration equations for TS, which could have led to incomplete deattenuation of the risk estimates.

PMCID: PMC6166207 [Available on 2019-10-01]
PMID: 29868784

J Cardiol. 2018 Oct;72(4):307-313.

Mendelian randomization: Its impact on cardiovascular disease.

Kawashiri MA(1), Tada H(2), Nomura A(2), Yamagishi M(2).

Cardiovascular diseases and their risk factors are inheritable. Single nucleotide polymorphisms in the human genome are found in around 1 in 1000 base pairs, and this may affect the genetic variety of individuals. During meiosis, any genetic information is randomized and is independent of other characteristics. In a Mendelian randomization study (MRS), a genetic variant associated with biomarker is used as a proxy for the biomarker, and the outcomes are compared between the groups harboring the effect alleles and a group with the reference allele. An MRS using variants of both rare and modest effect sizes and variants of common and lower effect sizes provides an understanding of risk factors and their causality of cardiovascular disease; for example, an individual possessing an allele associated with lower low-density lipoprotein cholesterol (LDL-C) exhibits lower risk of coronary artery disease (CAD). Moreover, the log-transformed reduction rates of CAD are linearly correlated with the reduction value of LDL-C. High-density lipoprotein (HDL) removes cholesteryl esters from peripheral tissues, including atherosclerotic plaque to the liver. Numerous epidemiological studies have shown that HDL-cholesterol (HDL-C) levels are inversely associated with the frequency of the occurrence of CAD. However, genetic variants, which are only associated with higher HDL-C levels, do not decrease the frequency of myocardial infarction. This fact shows that HDL-C level is not a cause but a biomarker of CAD. Discoveries of rare variants in Mendelian disorders resulted in the successful development of drugs for the general population. An MRS may also predict the pharmacological effectiveness and adverse side effects of novel drugs targeting specific molecules. An MRS could become a standard process to be performed before the development of novel drugs. Furthermore, future guidelines for the prevention of CAD should consider the genetic information of individuals, which will result in precision medicine for cardiovascular diseases.

PMID: 29801689

Diabetes Metab Syndr. 2018 Nov;12(6):885-891.

Cardiovascular risk factors: Is the metabolic syndrome related to aging? Epidemiology in a Portuguese population.

Ribeiro AS, Seixas R, Gálvez JM, Climent V.

AIMS: The primary objective of our study is to determine the prevalence of the metabolic syndrome in the population. The secondary objective is to determine the prevalence of cardiovascular risk factors, anthropometric alterations and the prevalence of target organ damage and their relationship with aging.
MATERIAL AND METHODS: The sample for the study was obtained by means of a consecutive population-based demonstration in 803 adults over 18 years of age belonging to the labor force of the company Grupo Delta SA. The study was carried out according to the guidelines of the Declaration of Helsinki. The individuals included in the study voluntarily participated, once informed of the purpose of the study, giving their prior verbal consent, to the company's human resources department, in the case of Delta Group workers.
RESULTS: 23.8% of the population has metabolic syndrome more prevalent in males, no smoking, no significant alcohol consumption, sedentary, with a high Body mass index (BMI). Its prevalence increases with age.
CONCLUSION: We found that the prevalence of metabolic syndrome increases with age and is present in people of working age, increasing the risk of cardiovascular diseases, work-related absences, and socio-economic costs.

PMID: 29778667 [Indexed for MEDLINE]

Alzheimers Dement. 2018 Nov;14(11):1406-1415

Midlife vascular risk factors and midlife cognitive status in relation to prevalence of mild cognitive impairment and dementia in later life: The Atherosclerosis Risk in Communities Study.

Knopman DS, Gottesman RF, Sharrett AR, Tapia AL, DavisThomas S, Windham BG, Coker L, Schneider ALC, Alonso A, Coresh J, Albert MS, Mosley TH Jr.

INTRODUCTION: The interplay between midlife vascular risk factors and midlife cognitive function with later life mild cognitive impairment (MCI) and dementia (DEM) is not well understood.
METHODS: In the Atherosclerosis Risk in Communities Study, cardiovascular risk factors and cognition were assessed in midlife, ages 45-64 years. In 2011-2013, 20-25 years later, all consenting Atherosclerosis Risk in Communities participants underwent a cognitive and neurological evaluation and were given adjudicated diagnoses of cognitively normal, MCI, or DEM.
RESULTS: In 5995 participants with complete covariate data, midlife diabetes, hypertension, obesity, and hypercholesterolemia were associated with late-life MCI and DEM. Low midlife cognition function was also associated with greater likelihood of late-life MCI or DEM. Both midlife vascular risk factors and midlife cognitive function remained associated with later life MCI or DEM when both were in the model.
DISCUSSION: Later life MCI and DEM were independently associated with midlife vascular risk factors and midlife cognition.

PMCID: PMC6231996 [Available on 2019-11-01]
PMID: 29763593

Semin Arthritis Rheum. 2018 Dec;48(3):367-373

Cardiovascular risk factors predicting cardiac events are different in patients with rheumatoid arthritis, psoriatic arthritis, and psoriasis.

Cooksey R, Brophy S, Kennedy J, Gutierrez FF, Pickles T, Davies R, Piguet V, Choy E.

OBJECTIVES: Increased cardiovascular risk in rheumatoid arthritis (RA) is well established. Examining traditional cardiovascular risk factors alone underestimates cardiovascular risk in RA. Systematic inflammation, measured by erythrocyte sedimentation rate or C-reactive protein is also a major risk factor. However, the contribution of traditional cardiovascular risk factors (such as obesity and hyperlipidaemia) compared to inflammation is uncertain in psoriatic arthritis (PsA) and RA. We examine the incidence of major adverse cardiac events (MACE) among patients with RA, PsA psoriasis, and controls adjusting for risk factors, inflammation and disease modifying anti-rheumatic drug treatment, to better define cardiovascular risk.

METHODS: Using the Secure Anonymised Information Linkage databank, comprising routinely collected Welsh health data from 1999 to 2013, the incidence and first occurrence of a MACE in individuals with RA (n = 8650), PsA (n = 2128) and psoriasis (n = 24,630) compared to controls (n = 11,87,706) was investigated.

RESULTS: Traditional cardiovascular risk factors are higher in RA, PsA and psoriasis than controls. After adjusting for these factors, additional cardiovascular risk was only significantly increased in female RA patients (HR = 1.3; 95% CI: 1.0-1.7; p = 0.05) and psoriasis (HR = 1.2; 95% CI: 1.0-1.4; p = 0.02) but not statistically significant for PsA (HR = 1.5; 95% CI: 0.9-2.5; p = 0.13). ESR and CRP were increased in patients with RA but not in patients with psoriasis.

CONCLUSION: Additional increased cardiovascular risk was observed in female RA and psoriasis but not PsA. Systematic inflammation is higher in RA but not psoriasis, indicating that there are varying mediators of cardiovascular risk across these conditions.

PMID: 29656791 [Indexed for MEDLINE]

Aten Primaria. 2018 Oct;50(8):459-466.

[Trends in the level of control of patients with type 2 diabetes from 2010 to 2015].

Herrero Gil AM, Pinillos Robles J, Sabio Repiso P, Martín Maldonado JL, Garzón González G, Gil de Miguel Á.

INTRODUCTION: Aim: To examine the trend in the level of control of glycated haemoglobin (HbA1c), blood pressure (BP), and LDL-cholesterol (LDL) in patients with type 2 diabetes mellitus between 2010 and 2015.
METHODS: Setting: 3 cut-offs in the years 2010, 2013, and 2015. Southeast area of Madrid.
DESIGN: Descriptive and cross-sectional epidemiological study.
PARTICIPANTS: Patients diagnosed and registered with type 2 diabetes. N=41,096 (2010), n=49,658 (2013), n=6,674 (2015) MAIN MEASUREMENTS: Measurement or not in the last year of HbA1c, BP, and LDL. Control of HbA1c (<7% individual targeting), BP (<140/90mmHg), and LDL (<100mg/dL, if cardiovascular disease <70mg/dL). Data were collected from electronic records of clinical history. The Chi-square test was used.
RESULTS: The percentages of patients with each parameter measured in 2010, 2013 and 2015 were: HbA1c: 36.4%, 37.0%, 62.0% (P<.001); BP: 33.2%, 43.3%, 65.0% (P<.001); LDL: 32.9%, 33.2%, 43.5% (P<.001). The percentages of patients with each parameter measured and controlled in 2010, 2013, and 2015 were: HbA1c: 59.6%, 59.1%, 79.6% (P<.001); BP: 74.9%, 67.4%, 79.2% (P<.001); LDL: 41.8%, 58.3%, 58.8% (P<.001)
CONCLUSION: In the 2010-2015 period, a sustained but insufficient trend of better control of HbA1c, BP and LDL was observed in patients with diabetes. The frequency of the measurements of these parameters improved more than the control of them. It seems that efforts to improve care for the patient with diabetes pay off, but they still have to be maintained.

PMID: 28838742

Outcomes Cardiovasculares

Pesquisa Bibliográfica efectuada em Pubmed (www.ncbi.nlm.nih.gov/ - Out a Dez 2018

AMA Netw Open. 2018 Dec 7;1(8):e186125.

Association of Second-line Antidiabetic Medications With Cardiovascular Events Among Insured Adults With Type 2 Diabetes.

O'Brien MJ, Karam SL, Wallia A, Kang RH, Cooper AJ, Lancki N, Moran MR, Liss DT, Prospect TA, Ackermann RT.

Importance: Understanding cardiovascular outcomes of initiating second-line antidiabetic medications (ADMs) may help inform treatment decisions after metformin alone is not sufficient or not tolerated. To date, no studies have compared the cardiovascular effects of all major second-line ADMs during this early decision point in the pharmacologic management of type 2 diabetes.

Objective: To examine the association of second-line ADM classes with major adverse cardiovascular events.

Design, Setting, and Participants: Retrospective cohort study among 132 737 insured adults with type 2 diabetes who started therapy with a second-line ADM after taking either metformin alone or no prior ADM. This study used 2011-2015 US nationwide administrative claims data. Data analysis was performed from January 2017 to October 2018.

Exposures: Dipeptidyl peptidase 4 (DPP-4) inhibitors, glucagon-like peptide-1 (GLP-1) receptor agonists, sodium-glucose cotransporter 2 (SGLT-2) inhibitors, thiazolidinediones (TZDs), basal insulin, and sulfonylureas or meglitinides (both referred to as sulfonylureas hereafter). The DPP-4 inhibitors served as the comparison group in all analyses.

Main Outcomes and Measures: The primary outcome was time to first cardiovascular event after starting the second-line ADM. This composite outcome was based on hospitalization for the following cardiovascular conditions: congestive heart failure, stroke, ischemic heart disease, or peripheral artery disease.

Results: Among 132 737 insured adult patients with type 2 diabetes (men, 55%; aged 45-64 years, 58%; white, 63%), there were 3480 incident cardiovascular events during 169 384 person-years of follow-up. Patients were censored after the first cardiovascular event, discontinuation of insurance coverage, transition from International Classification of Diseases, Ninth Revision (ICD-9) to end of ICD-9 coding, or 2 years of follow-up. After adjusting for patient, prescriber, and health plan characteristics, the risk of composite cardiovascular events after starting GLP-1 receptor agonists was lower than DPP-4 inhibitors (hazard ratio [HR], 0.78; 95% CI, 0.63-0.96), but this finding was not significant in all sensitivity analyses. Cardiovascular event rates after starting treatment with SGLT-2 inhibitors (HR, 0.81; 95% CI, 0.57-1.53) and TZDs (HR, 0.92; 95% CI, 0.76-1.11) were not statistically different from DPP-4 inhibitors. The comparative risk of cardiovascular events was higher after starting treatment with sulfonylureas

(HR, 1.36; 95% CI, 1.23-1.49) or basal insulin (HR, 2.03; 95% CI, 1.81-2.27) than DPP-4 inhibitors.

Conclusions and Relevance: Among insured adult patients with type 2 diabetes initiating second-line ADM therapy, the short-term cardiovascular outcomes of GLP-1 receptor agonists, SGLT-2 inhibitors, and DPP-4 inhibitors were similar. Higher cardiovascular risk was associated with use of sulfonylureas or basal insulin compared with newer ADM classes. Clinicians may consider prescribing GLP-1 receptor agonists, SGLT-2 inhibitors, or DPP-4 inhibitors more routinely after metformin rather than sulfonylureas or basal insulin.

PMCID: PMC6324353
PMID: 30646315

Eur Heart J. 2018 Dec 24.

Resting heart rate and cardiovascular outcomes in diabetic and non-diabetic individuals at high cardiovascular risk analysis from the ONTARGET/TRANSCEND trials.

Böhm M, Schumacher H, Teo KK, Lonn EM, Mahfoud F, Ukena C, Mann JFE, Mancia G, Redon J, Schmieder RE, Sliwa K, Marx N, Weber MA, Williams B, Yusuf S.

Aims: Resting heart rate (RHR) has been shown to be associated with cardiovascular outcomes in various conditions. It is unknown whether different levels of RHR and different associations with cardiovascular outcomes occur in patients with or without diabetes, because the impact of autonomic neuropathy on vascular vulnerability might be stronger in diabetes.

Methods and results: We examined 30 937 patients aged 55 years or older with a history of or at high risk for cardiovascular disease and after myocardial infarction, stroke, or with proven peripheral vascular disease from the ONTARGET and TRANSCEND trials investigating ramipril, telmisartan, and their combination followed for a median of 56 months. We analysed the association of mean achieved RHR on-treatment with the primary composite outcome of cardiovascular death, myocardial infarction, stroke, hospitalization for heart failure, the components of the composite primary outcome, and all-cause death as continuous and categorical variables. Data were analysed by Cox regression analysis, ANOVA, and $\chi 2$ test. These trials were registered with ClinicalTrials.gov.number NCT00153101. Patients were recruited from 733 centres in 40 countries between 1 December 2001 and 31 July 2008 (ONTARGET) and 1 November 2001 until 30 May 2004 (TRANSCEND). In total, 19 450 patients without diabetes and 11 487 patients with diabetes were stratified by mean RHR. Patients with diabetes compared to no diabetes had higher RHRs (71.8 ± 9.0 vs. 67.9 ± 8.8, $P < 0.0001$). In the categories of <60 bpm, 60 ≤ 65 bpm, 65 ≤ 70 bpm, 70 ≤ 75 bpm, 75 ≤ 80 bpm and ≥80 bpm, non-diabetic patients had an increased hazard of the primary outcome with mean RHR of 75 ≤ 80 bpm (adjusted hazard ratio [HR] 1.17 (1.01-1.36)) compared to RHR 60 ≤ 65 bpm. For patients with in-trial RHR ≥80 bpm the hazard ratios were highest (diabetes: 1.96 (1.64-2.34), no diabetes: 1.73 (1.49-2.00), For cardiovascular death hazards were also clearly increased at RHR ≥80 bpm (diabetes [1.99, (1.53-2.58)], no diabetes [1.73 (1.38-2.16)]. Similar results were obtained for hospitalization for heart failure and all-cause death while the effect of RHR on myocardial infarction and stroke was less pronounced. Results were robust after adjusting for various risk indicators including beta-blocker use and atrial fibrillation. No significant association to harm was observed at lower RHR.

Conclusion: Mean RHR above 75-80 b.p.m. was associated with increased risk for cardiovascular outcomes except for stroke. Since in diabetes, high RHR is associated with

higher absolute event numbers and patients have higher RHRs, this association might be of particular clinical importance in diabetes. These data suggest that RHR lowering in patients with RHRs above 75-80 b.p.m. needs to be studied in prospective trials to determine if it will reduce outcomes in diabetic and non-diabetic patients at high cardiovascular risk.

Clinical Trial registration: http://clinicaltrials.gov.Unique identifier:
NCT00153101.

PMID: 30590564

J Allergy Clin Immunol. 2018 Dec 18. pii: S0091-6749(18)32728-3.

Atopic eczema and major cardiovascular outcomes: A systematic review and meta-analysis of population-based studies.

Ascott A, Mulick A, Yu AM, Prieto-Merino D, Schmidt M, Abuabara K, Smeeth L, Roberts A, Langan SM.

BACKGROUND: Atopic eczema is a common inflammatory skin disease. Various inflammatory conditions have been linked to cardiovascular disease, a major cause of global mortality and morbidity.
OBJECTIVE: We sought to systematically review and meta-analyze population-based studies assessing associations between atopic eczema and specific cardiovascular outcomes.
METHODS: MEDLINE, Embase, and Global Health were searched from inception to December 2017. We obtained pooled estimates using random-effects meta-analyses. We used a multivariate Bayesian meta-regression model to estimate the slope of effect of increasing atopic eczema severity on cardiovascular outcomes.
RESULTS: Nineteen relevant studies were included. The effects of atopic eczema reported in cross-sectional studies were heterogeneous, with no evidence for pooled associations with angina, myocardial infarction, heart failure, or stroke. In cohort studies atopic eczema was associated with increased risk of myocardial infarction (n = 4; relative risk [RR], 1.12; 95% CI, 1.00-1.25), stroke (n = 4; RR, 1.10; 95% CI, 1.03-1.17), ischemic stroke n = 4; RR, 1.17; 95% CI, 1.14-1.20), angina (n = 2; RR, 1.18; 95% CI, 1.13-1.24), and heart failure (n = 2; RR, 1.26; 95% CI, 1.05-1.51). Prediction intervals were wide for myocardial infarction and stroke. The risk of cardiovascular outcomes appeared to increase with increasing severity (mean RR increase between severity categories, 1.15; 95% credibility interval, 1.09-1.21; uncertainty interval, 1.04-1.28).
CONCLUSION: Significant associations with cardiovascular outcomes were more common in cohort studies but with considerable between-study heterogeneity. Increasing atopic eczema severity was associated with increased risk of cardiovascular outcomes. Improved awareness among stakeholders regarding this small but significant association is warranted.

PMID: 30576754

Nutrients. 2018 Dec 19;10(12). pii: E2012.

Erythrocyte n-6 Fatty Acids and Risk for Cardiovascular Outcomes and Total Mortality in the Framingham Heart Study.

Harris WS, Tintle NL, Ramachandran VS.

BACKGROUND: The prognostic value of erythrocyte levels of n-6 fatty acids (FAs) for total mortality and cardiovascular disease (CVD) outcomes remains an open question.
METHODS: We examined cardiovascular (CV) outcomes and death in 2500 individuals in the Framingham Heart Study Offspring cohort without prevalent CVD (mean age 66 years, 57% women) as a function of baseline levels of different length n-6 FAs (18 carbon, 20 carbon, and 22 carbon) in the erythrocyte membranes. Clinical outcomes were monitored for up to 9.5 years (median follow up, 7.26 years). Cox proportional hazards models were adjusted for a variety of demographic characteristics, clinical status, and red blood cell (RBC) n-6 and long chain n-3 FA content.
RESULTS: There were 245 CV events, 119 coronary heart disease (CHD) events, 105 ischemic strokes, 58 CVD deaths, and 350 deaths from all causes. Few associations between either mortality or CVD outcomes were observed for n-6 FAs, with those that were observed becoming non-significant after adjusting for n-3 FA levels.
CONCLUSIONS: Higher circulating levels of marine n-3 FA levels are associated with reduced risk for incident CVD and ischemic stroke and for death from CHD and all-causes; however, in the same sample little evidence exists for association with n-6 FAs. Further work is needed to identify a full profile of FAs associated with cardiovascular risk and mortality.

PMCID: PMC6316092
PMID: 30572606

J Am Heart Assoc. 2018 Dec 4;7(23):e011367.

Anti-Inflammatory Effects of a Vegan Diet Versus the American Heart Association-Recommended Diet in Coronary Artery Disease Trial.

Shah B, Newman JD, Woolf K, Ganguzza L, Guo Y, Allen N, Zhong J, Fisher EA, Slater J.

Background Dietary interventions may play a role in secondary cardiovascular prevention. hsCRP (High-sensitivity C-reactive protein) is a marker of risk for major adverse cardiovascular outcomes in coronary artery disease. Methods and Results The open-label, blinded end-point, EVADE CAD (Effects of a Vegan Versus the American Heart Association-Recommended Diet in Coronary Artery Disease) trial randomized participants (n=100) with coronary artery disease to 8 weeks of a vegan or American Heart Association-recommended diet with provision of groceries, tools to measure dietary intake, and dietary counseling. The primary end point was high-sensitivity C-reactive protein. A linear regression model compared end points after 8 weeks of a vegan versus American Heart Association diet and adjusted for baseline concentration of the end point. Significance levels for the primary and secondary end points were set at 0.05 and 0.0015, respectively. A vegan diet resulted in a significant 32% lower high-sensitivity C-reactive protein (β, 0.68, 95% confidence interval [0.49-0.94]; P=0.02) when compared with the American Heart Association diet. Results were consistent after adjustment for age, race, baseline waist circumference, diabetes mellitus, and prior myocardial infarction (adjusted β, 0.67 [0.47-0.94], P=0.02). The degree of reduction in body mass index and waist circumference did not significantly differ between the 2 diet groups (adjusted β, 0.99 [0.97-1.00], P=0.10; and adjusted β, 1.00 [0.98-1.01], P=0.66, respectively). There were also no significant differences in markers of glycemic control between the 2 diet groups. There was a nonsignificant 13% reduction in low-density lipoprotein cholesterol with the vegan diet when compared with the American Heart Association diet (adjusted β, 0.87 [0.78-0.97], P=0.01). There were no significant differences in other lipid parameters. Conclusions In patients with coronary artery disease on guideline-directed medical therapy, a vegan diet may be considered to lower high-sensitivity C-reactive protein as a risk marker of adverse outcomes.

Clinical Trial Registration URL : http://www.clinicaltrials.gov .
Unique identifier: NCT 02135939.

PMID: 30571591

Circ Cardiovasc Qual Outcomes. 2018 Nov;11(11):e004724.

Body Weight Variability and Cardiovascular Outcomes in Patients With Type 2 Diabetes Mellitus.

Bangalore S, Fayyad R, DeMicco DA, Colhoun HM, Waters DD.

BACKGROUND: Some studies have shown that body weight variability is a risk factor for cardiovascular events, but this has not been studied in subjects with diabetes mellitus.
METHODS AND RESULTS: We measured intraindividual variations in body weight from baseline and follow-up visits in 6408 subjects with type 2 diabetes mellitus from 3 clinical trials. The primary end point, any coronary event, was a composite of coronary heart disease death, myocardial infarction, resuscitated cardiac arrest, coronary revascularization, and unstable or new-onset angina. After adjustment for risk factors, baseline lipid levels, mean body weight, and weight change, each increase of 1 SD in body weight variability, measured as average successive variability and used as a time-dependent covariate, was associated with an increase in the risk of any coronary event (hazard ratio, 1.08; 95% CI, 1.01-1.14; P=0.017), major coronary event (hazard ratio, 1.12; 95% CI, 1.04-1.20; P=0.002), any cardiovascular event (hazard ratio, 1.08; 95% CI, 1.03-1.14; P=0.0015), and death (hazard ratio, 1.16; 95% CI, 1.10-1.22; P<0.0001). Among patients in the quintile with the highest variation in body weight compared with the lowest, the risk of any coronary event was 59% higher; the risk of a major coronary event, 82% higher; any cardiovascular event, 75% higher; death, 82% higher; myocardial infarction, 99% higher; and stroke, 92% higher in adjusted models. The results were consistent in a number of sensitivity analyses.
CONCLUSIONS: Among subjects with type 2 diabetes mellitus, fluctuation in body weight was associated with higher mortality and a higher rate of cardiovascular events, independent of traditional cardiovascular risk factors.

CLINICAL TRIAL REGISTRATION: URL: http://www.clinicaltrials.gov .
Unique identifier: NCT00327691 and NCT00327418.

PMID: 30571333

Circulation. 2018 Dec 4;138(23):2627-2637.

Associations of Variability in Blood Pressure, Glucose and Cholesterol Concentrations, and Body Mass Index With Mortality and Cardiovascular Outcomes in the General Population.

Kim MK, Han K, Park YM, Kwon HS, Kang G, Yoon KH, Lee SH.

BACKGROUND: Variability in metabolic parameters, such as fasting blood glucose and cholesterol concentrations, blood pressure, and body weight can affect health outcomes. We investigated whether variability in these metabolic parameters has additive effects on the risk of mortality and cardiovascular outcomes in the general population.
METHODS: Using nationally representative data from the Korean National Health Insurance System, 6748773 people who were free of diabetes mellitus, hypertension, and dyslipidemia and who underwent ≥3 health examinations from 2005 to 2012 were followed to the end of 2015. Variability in fasting blood glucose and total cholesterol concentrations, systolic blood pressure, and body mass index was measured using the coefficient of variation, SD, variability independent of the mean, and average real variability. High variability was defined as the highest quartile of variability. Participants were classified numerically according to the number of high-variability parameters (eg, a score of 4 indicated high variability in all 4 metabolic parameters). Cox proportional hazards models adjusting for age, sex, smoking, alcohol, regular exercise, income, and baseline levels of fasting blood glucose, systolic blood pressure, total cholesterol, and body mass index were used.
RESULTS: There were 54785 deaths (0.8%), 22498 cases of stroke (0.3%), and 21452 myocardial infarctions (0.3%) during a median follow-up of 5.5 years. High variability in each metabolic parameter was associated with a higher risk for all-cause mortality, myocardial infarction, and stroke. Furthermore, the risk of outcomes increased significantly with the number of high-variability metabolic parameters. In the multivariable-adjusted model comparing a score of 0 versus 4, the hazard ratios (95% CIs) were 2.27 (2.13-2.42) for all-cause mortality, 1.43 (1.25-1.64) for myocardial infarction, and 1.41 (1.25-1.60) for stroke. Similar results were obtained when modeling the variability using the SD, variability independent of the mean, and average real variability, and in various sensitivity analyses.
CONCLUSIONS: High variability of fasting blood glucose and total cholesterol levels, systolic blood pressure, and body mass index was an independent predictor of mortality and cardiovascular events. There was a graded association between the number of high-variability parameters and cardiovascular outcomes.

PMID: 30571256

Sao Paulo Med J. 2018 Dec 13. pii: S1516-31802018005017101.

Central hemodynamic parameters to predict cardiovascular outcomes and mortality among the elderly: protocol for a systematic review.

Sausen G(1), Vieceli T(2), Rodrigues CG(3), Kipper D(4), Stein AT(5), Grezzana GB(6).

BACKGROUND: Central blood pressure is a factor that may predict cardiovascular events. However, its use in clinical practice is not well consolidated. Therefore, the aim of our study will be to summarize the use of central hemodynamic parameters to predict cardiovascular-related outcomes and all-cause mortality.
DESIGN AND SETTING: Protocol for systematic review of longitudinal observational studies conducted in healthcare institutions, as presented in the studies included.
METHODS: We will perform a systematic search in the electronic databases MEDLINE (via PubMed), EMBASE and LILACS (via Virtual Health Library (VHL)), using health descriptors terms for elderly people and for hemodynamic indices of central blood pressure. We will include articles that evaluated hemodynamic indices and at least one of the following outcomes: all-cause mortality, total cardiovascular death, total non-cardiovascular death, myocardial infarction, stroke, coronary artery restenosis after percutaneous coronary intervention, revascularization and aortic syndromes. Two independent reviewers will conduct analysis on the abstracts selected and on the full-text articles. Two reviewers will independently perform data extraction and evaluate the methodological quality of the articles selected, and a third reviewer will evaluate any divergences. The methodological quality of the studies will be assessed in accordance with the ROBINS-I tool (Risk Of Bias In Non-randomized Studies of Interventions).
RESULTS AND CONCLUSIONS: Through this systematic review, we intend to summarize evidence that supports the use of central hemodynamic parameters for central blood pressure to diagnose and perform prognostics on arterial hypertension in elderly patients within clinical practice and predict future cardiovascular events in this population.

REGISTRATION: Prospero - CRD42018085264.
PMID: 30569954

Circ Heart Fail. 2018 Dec;11(12):e005266.

Thyroid Dysfunction in Heart Failure and Cardiovascular Outcomes.

Kannan L Shaw PA, Morley MP, Brandimarto J, Fang JC, Sweitzer NK, Cappola TP, Cappola AR.

BACKGROUND: The effects of thyroid dysfunction in patients with preexisting heart failure have not been adequately studied. We examined the prevalence of thyroid dysfunction and associations with cardiovascular outcomes in a large, prospective cohort of outpatients with preexisting heart failure.

METHODS AND RESULTS: We examined associations between thyroid dysfunction and New York Heart Association class, atrial fibrillation, and a composite end point of ventricular assist device placement, heart transplantation, or death in 1365 participants with heart failure enrolled in the Penn Heart Failure Study. Mean age was 57 years, 35% were women, and the majority had New York Heart Association class II (45%) or III (32%) symptoms. More severe heart failure was associated with higher thyroid-stimulating hormone (TSH), higher free thyroxine (FT4), and lower total triiodothyronine (TT3) concentrations ($P<0.001$ all models). Atrial fibrillation was positively associated with higher levels of FT4 alone ($P\leq0.01$ all models). There were 462 composite end points over a median 4.2 years of follow-up. In adjusted models, compared with euthyroidism, subclinical hypothyroidism (TSH 4.51-19.99 mIU/L with normal FT4) was associated with an increased risk of the composite end point overall (hazard ratio, 1.82; 95% CI, 1.27-2.61; $P=0.001$) and in the subgroup with TSH ≥7.00 mIU/L (hazard ratio, 3.25; 95% CI, 1.96-5.39; $P<0.001$), but not in the subgroup with TSH 4.51-6.99 mIU/L (hazard ratio, 1.26; 95% CI, 0.78-2.06; $P=0.34$). Isolated low T3 was also associated with the composite end point (hazard ratio, 2.12; 95% CI, 1.65-2.72; $P<0.001$).

CONCLUSIONS: In patients with preexisting heart failure, subclinical hypothyroidism with TSH ≥7 mIU/L and isolated low T3 levels are associated with poor prognosis. Clinical trials are needed to explore therapeutic effects of T4 and T3 administration in heart failure.

PMID: 30562095

Medicine (Baltimore). 2018 Dec;97(50):e13246.

Weight reduction and cardiovascular benefits: Protocol for a systematic review and meta-analysis.

Zhao Y, Yu BY, Liu Y, Tong T, Liu Y.

BACKGROUND: There is widespread obesity paradox in cardiovascular diseases, the cardiovascular influence from weight management remains controversial. Moreover, previous publications indicating that different weight reduction extent might lead to various results. Thus, it is of importance to reassess the cardiovascular benefits of weight management strategies.
OBJECTIVES: This review is designed to assess the association between weight loss and cardiovascular outcomes.
METHODS: Clinical trials including randomized control trials, observational studies reported a weight change before and after weight interventions including lifestyle intervention, as well as pharmacotherapies were included. Three major databases will be searched to retrieve the appropriate studies. Dual selection and abstraction of data will be conducted by 2 authors independently. The population, intervention, comparator, outcomes, study characteristics framework will be used to extract all the necessary data from included studies. The risk of bias assessment will be conducted in duplicate based on the Cochrane risk of bias guideline for randomized controlled trials (RCTs) and the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement for observational studies respectively. The primary outcomes will be the cardiovascular mortality, and the secondary outcomes are all-cause mortality and new cardiovascular events. A meta-analysis will be considered if there is sufficient homogeneity among selected studies. Follow the criteria of Grading of Recommendations, Assessment, Development and Evaluation (GRADE), the quality of the cumulative evidence will be evaluated.
RESULTS AND CONCLUSIONS: The results of this systematic review could provide reliable and concrete evidence for weight loss and its cardiovascular benefits.

Prospero registration number: CRD42018108582.

PMID: 30557969 [Indexed for MEDLINE]

Rev Port Cardiol. 2018 Dec;37(12):961-969.

Impact on long-term cardiovascular outcomes of different cardiac resynchronization therapy response criteria.

Rodrigues I, Abreu A, Oliveira M, Cunha PS, Clara HS, Osório P, Lousinha A, Valente B, Portugal G, Rio P, Morais LA, Santos V, Carmo MM, Ferreira RC.

INTRODUCTION: There is a lack of consensus on the definition of response to cardiac resynchronization therapy (CRT), and it is not clear which response criteria have most influence on cardiac event-free survival.
OBJECTIVES: To assess the predictive value of various response criteria in patients undergoing CRT and the agreement between them.
METHODS: We performed a secondary analysis of the BETTER-HF trial. Patient response was classified at six months after CRT according to eleven criteria used in previous trials. The predictive value of response criteria for survival free from mortality, cardiac transplantation and heart failure hospitalization was assessed by Cox regression analysis. Agreement between the different response criteria was assessed using Cohen's kappa (κ).
RESULTS: A total of 115 patients were followed for a mean of 25 months. During follow-up, 15 deaths occurred (13%) and 29 patients had at least one adverse cardiac event (25%). Only five of the eleven response criteria were predictors of event-free survival. The most powerful isolated clinical and echocardiographic predictors were a reduction of ≥1 NYHA functional class (HR 0.39 for responders; 95% CI 0.18-0.83, p=0.014) and an increase of at least 15% in left ventricular ejection fraction (HR 0.43, 95% CI 0.20-0.90, p=0.024), respectively. Agreement between the different response criteria was poor.
CONCLUSIONS: Most currently used response criteria do not predict clinical outcomes and have poor agreement. It is essential to establish a consensus on the definition of CRT response in order to standardize studies.

PMID: 30545744

PLoS One. 2018 Dec 13;13(12):e0208817.

Relationship of body mass index and waist circumference with clinical outcomes following percutaneous coronary intervention.

Lee Y, Jin U, Lee WM, Lim HS, Lim YH.

BACKGROUND: A biphasic, U-shape relationship has been reported between body mass index (BMI) and clinical outcomes following percutaneous coronary intervention (PCI). However, the relationship between waist circumference (WC) and the cardiovascular risk following PCI has not been reported.
METHODS: A prospective cohort study was performed. A major adverse cardiac event (MACE) was defined as a composite of cardiac death (CD), nonfatal myocardial infarction (NFMI) and target vessel revascularization (TVR). Patients were evenly divided into 4 groups according to BMI (Q1BMI, Q2BMI, Q3BMI and Q4BMI) and WC (Q1WC, Q2WC, Q3WC and Q4WC).
RESULTS: A total of 1,421 patients were observed for 5 years. The risk of the composite events of CD and NFMI (CD/NFMI) was lower in the Q3WC and Q4WC groups than in the Q1WC group, whereas it was only marginally lower in the Q2BMI group than in the Q1BMI group (ANOVA, p = 0.062). The risk of MACE was highest in the Q1WC group and lowest in the Q3WC group; however, the risk of MACE did not differ among the 4 groups, according to BMI. Multivariate Cox-regression analyses showed that the risk of CD/NFMI gradually decreased with BMI (linear p = 0.030) and with WC (linear p = 0.015). The risks of TVR and MACEs that were driven by TVRs showed a distinguishing biphasic, U-shaped relationship with WC (nonlinear p = 0.009) but not with BMI (nonlinear p = 0.439). Landmark survival analysis showed that the incidences of CD and NFMI were higher in the lower BMI groups and lower WC groups than in the higher BMI groups and higher WC groups, respectively, until 1 year and did not differ afterward. In contrast, the incidence of MACE was highest in Q1WC and lowest in Q3WC (log-rank p = 0.003), whereas the incidence was not different among the groups according to BMI.
CONCLUSIONS: Both BMI and WC were associated with a lower risk of early episodes of CD and NFMI after PCI. In the late period after PCI, WC demonstrated a biphasic, U-shaped association between cardiovascular outcomes and adiposity, whereas BMI did not.

PMCID: PMC6292633
PMID: 30543687

Cardiol Rev. 2018 Dec 7.. [Epub ahead of print]

Cardiovascular Effects of Drugs Used to Treat Attention Deficit/Hyperactivity Disorder Part 2: Impact on Cardiovascular Events and Recommendations for Evaluation and Monitoring.

Fay TB, Alpert MA.

A variety of psychostimulant and non-psychostimulant medications have proven to be successful in reducing inattention, impulsivity and hyperactivity in individuals with attention-deficit/hyperactivity disorder with (ADHD). Psychostimulants used to treat ADHD include methylphenidate and related drugs and various amphetamine preparations. Non-psychostimulant medications used to treat ADHD include atomoxetine and two alpha-2 adrenergic agonists; guanfacine extended-release and clonidine extended-release. The psychostimulants and atomoxetine have been shown, on average, to increase heart rate (HR) by 3-10 beats/min, systolic blood pressure by 3-8 mmHg, and diastolic BP by 2-14 mmHg. These drugs may also delay ventricular repolarization. The alpha-2 adrenergic agonists may reduce HR and BP. For these reasons, there is concern about the safety of psychostimulant and non-psychostimulant medications in patients with ADHD. Studies in healthy children adolescents and adults have not consistently shown a disproportionately high risk of major adverse cardiovascular outcomes including sudden unexpected death. Those with underlying cardiovascular disease have, in general, tolerated these drugs well. Certain high-risk groups have been identified who may benefit from cardiology consultation prior to drug initiation. Several American and Canadian professional societies have published guidelines for cardiovascular evaluation, management, and monitoring of patients with ADHD who are candidates for pharmacotherapy.

PMID: 30531411

Curr Drug Discov Technol. 2018 Dec 10. [Epub ahead of print]

PCSK9 inhibitors and cardiovascular disease: impact on cardiovascular outcomes.

Farmaki P, Damaskos C, Garmpis N, Garmpi A, Savvanis S, Diamantis E.

Cardiovascular disease (CAD) remains the leading cause of morbidity and mortality in the western world. Hypolipidemic drugs have long been used for the primary and secondary prevention of heart disease. However, the high frequency of recurrent events in patients despite on hypolipidemic therapy has increased the need for new more targeted therapeutic approaches. Proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors are monoclonal antibodies to the PCSK9 gene and represent a new class of drugs that have been shown to further decrease LDL-C when administered as a monotherapy or in combination with statins. In addition to LDL reduction, PCSK9 inhibitors are shown to decrease apolipoprotein B and lipoprotein(a) levels without major adverse effects. Whether or not PCSK9 inhibitors can actually reduce the incidence of cardiovascular events and ameliorate CAD prognosis is yet to be clarified. This review summarizes recent literature on the safety and efficacy of PCSK9 inhibitors on CAD outcome and its potential role in the management of patients with high-risk cardiovascular disease.

PMID: 30526464

Diabetes Obes Metab. 2018 Nov 28. [Epub ahead of print]

PCSK9 inhibitor therapy: A systematic review and meta-analysis of metabolic and cardiovascular outcomes in patients with diabetes.

Monami M, Sesti G, Mannucci E.

AIMS: Pro-protein convertase subtilisin/kexin type 9 (PCSK9) inhibitors bring about a wide reduction in low-density lipoprotein (LDL) cholesterol, greater than that of other lipid-lowering agents. The aim of this metanalysis was assessment of the effects of PCSK9 inhibitors on glucose metabolism, LDL cholesterol, cardiovascular morbidity and mortality in individuals with and without diabetes.
MATERIALS AND METHODS: A Medline and Clinicaltrials.gov search for eligible studies published before 1 December 2017 was performed. All randomized trials comparing PCSK-9 inhibitors with placebo or active drugs were included. Primary endpoints included (a) incident diabetes, fasting glucose and HbA1c, (b) LDL cholesterol at endpoint in patients with diabetes and in the total sample, and (c) major cardiovascular events (MACE) and mortality in individuals with and without diabetes.
RESULTS: A total of 38 trials was identified. The risk of incident diabetes was not increased by PCSK-9 inhibitors, vs placebo or any comparator. The reduction in LDL cholesterol vs placebo in patients with diabetes was 52.6 [41.3;63.8] mg/dL; the corresponding figure for all patients was 66.9 [62.4;71.3] mg/dL. Meta-regression analysis showed an inverse correlation between proportion of patients with diabetes and drug effect on LDL cholesterol in trials vs ezetimibe, but not in those vs placebo. In studies reporting data on MACE and mortality separately for individuals with and without diabetes, the effect of PCSK-9 did not appear to be affected by diabetes.
CONCLUSION: PCSK-9 inhibitors do not affect glucose metabolism. Their efficacy on LDL cholesterol and MACE in patients with diabetes does not seem to be very dissimilar to that observed in non-diabetic participants.

PMID: 30485622

J Am Heart Assoc. 2018 Dec 4;7(23):e010405.

Healthy Lifestyle During the Midlife Is Prospectively Associated With Less Subclinical Carotid Atherosclerosis: The Study of Women's Health Across the Nation.

Wang D, Jackson EA, Karvonen-Gutierrez CA, Elliott MR, Harlow SD, Hood MM, Derby CA, Sternfeld B, Janssen I, Crawford SL, Huang MH, El Khoudary SR, Chae CU, Baylin A.

Background Measures of subclinical atherosclerosis are predictors of future cardiovascular outcomes as well as of physical and cognitive functioning. The menopausal transition is associated with accelerated progression of atherosclerosis in women. The prospective association between a healthy lifestyle during the midlife and subclinical atherosclerosis is unclear.

Methods and Results Self-reported data on smoking, diet, and physical activity from 1143 women in the Study of Women's Health Across the Nation were used to construct a 10-year average Healthy Lifestyle Score (HLS) during the midlife. Markers of subclinical atherosclerosis were measured 14 years after baseline and included common carotid artery intima-media thickness (CCA - IMT), adventitial diameter (CCA - AD), and carotid plaque. The associations of average HLS with CCA - IMT and CCA - AD were estimated using linear models; the association of average HLS with carotid plaque was estimated using cumulative logit models. Average HLS was associated with smaller CCA - IMT and CCA - AD in the fully adjusted models (P=0.0031 and <0.001, respectively). Compared with participants in the lowest HLS level, those in the highest level had 0.024 mm smaller CCA - IMT (95% confidence interval: -0.048, 0.000), which equals 17% of the SD of CCA - IMT , and 0.16 mm smaller CCA - AD (95% confidence interval: -0.27, -0.04), which equals 24% of the SD of CCA - AD . Among the 3 components of the HLS, abstinence from smoking had the strongest association with subclinical atherosclerosis.

Conclusions Healthy lifestyle during the menopausal transition is associated with less subclinical atherosclerosis, highlighting the growing recognition that the midlife is a critical window for cardiovascular prevention in women.

PMID: 30482079

Acta Diabetol. 2018 Nov 19. [Epub ahead of print]

Cardiovascular and mortality events in type 2 diabetes cardiovascular outcomes trials: a systematic review with trend analysis.

Vetrone LM, Zaccardi F, Webb DR, Seidu S, Gholap NN, Pitocco D, Davies MJ, Khunti K.

AIMS: To investigate cardiovascular disease and mortality trends in control arm participants of diabetes cardiovascular outcome trials (CVOTs).
METHODS: We electronically searched CVOTs published before October 2017. Data on all-cause mortality, cardiovascular mortality and events, and baseline characteristics were collected, along with study calendar years. Trends were estimated using negative binomial regressions and reported as rate ratio (RR) per 5-year intervals.
RESULTS: 26 CVOTs, conducted from 1961 to 2015, included 86788 participants with 6543 all-cause deaths, 3265 cardiovascular deaths, and 7657 3-point major adverse cardiovascular events (3-P MACE; combined endpoint of cardiovascular death, nonfatal myocardial infarction, nonfatal stroke). In unadjusted analysis, there was an increasing trend for 3-P MACE rates over time (5-year RR 1.57; 95% CI 1.34, 1.84); a small increasing trend for cardiovascular disease mortality rates (1.13; 1.01, 1.26); and stable rates for all-cause death. Adjusting for age, sex, previous myocardial infarction, and diabetes duration, there was no evidence of trends for 3-P MACE or cardiovascular disease mortality rates, while reducing rates were observed for nonfatal myocardial infarction (5-year RR: 0.72; 0.54, 0.96), total stroke (0.76; 0.66, 0.88), and nonfatal stroke (0.60; 0.43, 0.82).
CONCLUSIONS: In contrast to real-world data, there was no evidence of an improvement in all-cause and cardiovascular mortality in type 2 diabetes participants included in control arms of randomised clinical trials across 5 decades. Further studies should investigate whether and how dissimilarities in populations, procedures, and assessments of exposures and outcomes explain the differences between real-world setting and clinical trials.

PMID: 30456728

J Am Coll Cardiol. 2018 Nov 3. pii: S0735-1097(18)39035-1.

AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines.

Wilson PWF, Polonsky TS, Miedema MD, Khera A, Kosinski AS, Kuvin JT.

BACKGROUND: The 2013 American College of Cardiology/American Heart Association guidelines for the treatment of blood cholesterol found little evidence to support the use of nonstatin lipid-modifying medications to reduce atherosclerotic cardiovascular disease (ASCVD) events. Since publication of these guidelines, multiple randomized controlled trials evaluating nonstatin lipid-modifying medications have been published.

METHODS: We performed a systematic review to assess the magnitude of benefit and/or harm from additional lipid-modifying therapies compared with statins alone in individuals with known ASCVD or at high risk of ASCVD. We included data from randomized controlled trials with a sample size of >1,000 patients and designed for follow-up >1 year. We performed a comprehensive literature search and identified 10 randomized controlled trials for intensive review, including trials evaluating ezetimibe, niacin, cholesterol-ester transfer protein inhibitors, and PCSK9 inhibitors. The prespecified primary outcome for this review was a composite of fatal cardiovascular events, nonfatal myocardial infarction, and nonfatal stroke.

RESULTS: The cardiovascular benefit of nonstatin lipid-modifying therapies varied significantly according to the class of medication. There was evidence for reduced ASCVD morbidity but not mortality with ezetimibe and 2 PSCK9 inhibitors. Reduced ASCVD mortality rate was reported for 1 PCSK9 inhibitor. The use of ezetimibe/simvastatin versus simvastatin in IMPROVE-IT (Improved Reduction of Outcomes: Vytorin Efficacy International Trial) reduced the primary outcome by 1.8% over 7 years (hazard ratio: 0.90; 95% CI: 0.84-0.96], 7-year number needed to treat: 56). The PSCK9 inhibitor evolocumab in the FOURIER study (Further Cardiovascular Outcomes Research with PCSK9 Inhibition in Subjects with Elevated Risk) decreased the primary outcome by 1.5% over 2.2 years (hazard ratio: 0.80; 95% CI: 0.73-0.88; 2.2=year number needed to treat: 67). In ODYSSEY OUTCOMES (Evaluation of Cardiovascular Outcomes After an Acute Coronary Syndrome During Treatment With Alirocumab), alirocumab reduced the primary outcome by 1.6% over 2.8 years (hazard ratio: 0.86; 95% CI: 0.79-0.93; 2.8-year number needed to treat: 63). For ezetimibe and the PSCK9 inhibitors, rates of musculoskeletal, neurocognitive, gastrointestinal, or other adverse event risks did not differ between the treatment and control groups. For patients at high risk of ASCVD already on background statin therapy, there was minimal evidence for improved ASCVD risk or adverse

events with cholesterol-ester transfer protein inhibitors. There was no evidence of benefit for the addition of niacin to statin therapy. Direct comparisons of the results of the 10 randomized controlled trials were limited by significant differences in sample size, duration of follow-up, and reported primary outcomes.

CONCLUSIONS: In a systematic review of the evidence for adding nonstatin lipid-modifying therapies to statins to reduce ASCVD risk, we found evidence of benefit for ezetimibe and PCSK9 inhibitors but not for niacin or cholesterol-ester transfer protein inhibitors.

PMID: 30423394

J Am Coll Cardiol. 2018 Dec 25;72(25):3233-3242.

Impact of Statins on Cardiovascular Outcomes Following Coronary Artery Calcium Scoring.

Mitchell JD, Fergestrom N, Gage BF, Paisley R, Moon P, Novak E, Cheezum M, Shaw LJ, Villines TC.

BACKGROUND: Compared with traditional risk factors, coronary artery calcium (CAC) scores improve prognostic accuracy for atherosclerotic cardiovascular disease (ASCVD) outcomes. However, the relative impact of statins on ASCVD outcomes stratified by CAC scores is unknown.

OBJECTIVES: The authors sought to determine whether CAC can identify patients most likely to benefit from statin treatment.

METHODS: The authors identified consecutive subjects without pre-existing ASCVD or malignancy who underwent CAC scoring from 2002 to 2009 at Walter Reed Army Medical Center. The primary outcome was first major adverse cardiovascular event (MACE), a composite of acute myocardial infarction, stroke, and cardiovascular death. The effect of statin therapy on outcomes was analyzed stratified by CAC presence and severity, after adjusting for baseline comorbidities with inverse probability of treatment weights based on propensity scores.

RESULTS: A total of 13,644 patients (mean age 50 years; 71% men) were followed for a median of 9.4 years. Comparing patients with and without statin exposure, statin therapy was associated with reduced risk of MACE in patients with CAC (adjusted subhazard ratio: 0.76; 95% confidence interval: 0.60 to 0.95; p = 0.015), but not in patients without CAC (adjusted subhazard ratio: 1.00; 95% confidence interval: 0.79 to 1.27; p = 0.99). The effect of statin use on MACE was significantly related to the severity of CAC (p < 0.0001 for interaction), with the number needed to treat to prevent 1 initial MACE outcome over 10 years ranging from 100 (CAC 1 to 100) to 12 (CAC >100).

CONCLUSIONS: In a largescale cohort without baseline ASCVD, the presence and severity of CAC identified patients most likely to benefit from statins for the primary prevention of cardiovascular diseases.

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PMID: 30409567

N Engl J Med. 2018 Nov 29;379(22):2097-2107.

Alirocumab and Cardiovascular Outcomes after Acute Coronary Syndrome.

Schwartz GG, Steg PG, Szarek M, Bhatt DL, Bittner VA, Diaz R, Edelberg JM, Goodman SG, Hanotin C, Harrington RA, Jukema JW, Lecorps G, Mahaffey KW, Moryusef A, Pordy R, Quintero K, Roe MT, Sasiela WJ, Tamby JF, Tricoci P, White HD, Zeiher AM; ODYSSEY OUTCOMES Committees and Investigators.

BACKGROUND: Patients who have had an acute coronary syndrome are at high risk for recurrent ischemic cardiovascular events. We sought to determine whether alirocumab, a human monoclonal antibody to proprotein convertase subtilisin-kexin type 9 (PCSK9), would improve cardiovascular outcomes after an acute coronary syndrome in patients receiving high-intensity statin therapy.

METHODS: We conducted a multicenter, randomized, double-blind, placebo-controlled trial involving 18,924 patients who had an acute coronary syndrome 1 to 12 months earlier, had a low-density lipoprotein (LDL) cholesterol level of at least 70 mg per deciliter (1.8 mmol per liter), a non-high-density lipoprotein cholesterol level of at least 100 mg per deciliter (2.6 mmol per liter), or an apolipoprotein B level of at least 80 mg per deciliter, and were receiving statin therapy at a high-intensity dose or at the maximum tolerated dose. Patients were randomly assigned to receive alirocumab subcutaneously at a dose of 75 mg (9462 patients) or matching placebo (9462 patients) every 2 weeks. The dose of alirocumab was adjusted under blinded conditions to target an LDL cholesterol level of 25 to 50 mg per deciliter (0.6 to 1.3 mmol per liter). The primary end point was a composite of death from coronary heart disease, nonfatal myocardial infarction, fatal or nonfatal ischemic stroke, or unstable angina requiring hospitalization.

RESULTS: The median duration of follow-up was 2.8 years. A composite primary end-point event occurred in 903 patients (9.5%) in the alirocumab group and in 1052 patients (11.1%) in the placebo group (hazard ratio, 0.85; 95% confidence interval [CI], 0.78 to 0.93; P<0.001). A total of 334 patients (3.5%) in the alirocumab group and 392 patients (4.1%) in the placebo group died (hazard ratio, 0.85; 95% CI, 0.73 to 0.98). The absolute benefit of alirocumab with respect to the composite primary end point was greater among patients who had a baseline LDL cholesterol level of 100 mg or more per deciliter than among patients who had a lower baseline level. The incidence of adverse events was similar in the two groups, with the exception of local injection-site reactions (3.8% in the alirocumab group vs. 2.1% in the placebo group).

CONCLUSIONS: Among patients who had a previous acute coronary syndrome and who were receiving high-intensity statin therapy, the risk of recurrent ischemic cardiovascular events was lower among those who received alirocumab than among those who received placebo.

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ODYSSEY OUTCOMES ClinicalTrials.gov number, NCT01663402 .).

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Average Clinician-Measured Blood Pressures and Cardiovascular Outcomes in Patients With Type 2 Diabetes Mellitus and Ischemic Heart Disease in the EXAMINE Trial.

White WB, Jalil F, Cushman WC, Bakris GL, Bergenstal R, Heller SR, Liu Y, Mehta C, Zannad F, Cannon CP.

Background Blood pressure (BP) treatment goals in patients with diabetes mellitus and increased cardiovascular risk remain controversial. Our study objective was to determine cardiovascular outcomes according to achieved BP s over the average follow-up period in the EXAMINE (Examination of Cardiovascular Outcomes With Alogliptin Versus Standard of Care) trial. Methods and Results EXAMINE was a cardiovascular outcomes trial in 5380 patients with type 2 diabetes mellitus and recent acute coronary syndromes. Risks of major adverse cardiac events and cardiovascular death or heart failure were analyzed using a Cox proportional hazards model with adjustment for baseline covariates in 10-mm Hg increments of clinician-measured systolic BP from ≤100 to >160 mm Hg and diastolic BP from ≤60 to >100 mm Hg averaged during the 24 months after randomization. Based on 2015 guidelines from the American College of Cardiology, the American Heart Association and the American Society of Hypertension and 2017 American Diabetes Association guidelines, systolic BP s of 131 to 140 mm Hg and diastolic BP s of 81 to 90 mm Hg were the reference groups. A U-shaped relationship between cardiovascular outcomes and BP s was observed. Importantly, compared with the systolic BP reference group, adjusted hazard ratios for major adverse cardiac events and cardiovascular death or heart failure were significantly higher in patients with systolic BP s <130 mm Hg. Similarly, compared with the diastolic BP reference group, adjusted hazard ratios for major adverse cardiac events and for cardiovascular death or heart failure were Significantly higher for diastolic BP s <80 mm Hg. Conclusions In patients with type 2 diabetes mellitus and recent acute coronary syndrome, average BP s <130/80 mm Hg were associated with worsened cardiovascular outcomes. These data suggest that intensive control of BP in patients with type 2 diabetes mellitus and ischemic heart disease should be evaluated in a prospective randomized trial.

Clinical Trial Registration URL : https://www.clinicaltrials.gov .
Unique identifier: NCT 00968708.

PMID: 30371278

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Validating Publicly Available Crosswalks for Translating ICD-9 to ICD-10 Diagnosis Codes for Cardiovascular Outcomes Research.

Columbo JA, Kang R, Trooboff SW, Jahn KS, Martinez J, Moore KO, Austin AM, Morden NE, Brooks CG, Skinner JS, Goodney PP

Background On October 1, 2015, the Center for Medicare and Medicaid Services transitioned from the International Classification of Diseases, Ninth Revision (ICD-9) to the ICD, Tenth Revision (ICD-10) compendium of codes for diagnosis and billing in health care, but translation between the two is often inexact. Here we describe a validated crosswalk to translate ICD-9 codes into ICD-10 codes, with a focus on complications after carotid revascularization and endovascular aortic aneurysm repair.

Methods and Results We devised an 8-step process to derive and validate ICD-10 codes from existing ICD-9 codes. We used publicly available sources, including the General Equivalence Mapping database, to translate ICD-9 codes used in prior work to ICD-10 codes. We defined ICD-10 codes as validated if they were concordant with the initial ICD-9 codes after manual comparison by two physicians. Our primary validation measure was the percent of valid ICD-10 codes out of the total ICD-10 codes obtained during translation. We began with 126 ICD-9 diagnosis codes used for complication identification after carotid revascularization procedures, and 97 ICD-9 codes for complications after endovascular aortic aneurysm procedures. Translation generated 143 ICD-10 codes for carotid revascularization, a 14% increase from the initial 126 codes. Manual comparison demonstrated 98% concordance, with 99% agreement between the reviewers. Similarly, we identified 108 ICD-10 codes for endovascular aortic aneurysm repair, an 11% increase from the initial 97 ICD-9 codes. We again noted excellent concordance and agreement (98% and 100%, respectively). Manual review identified 4 ICD-10 codes incorrectly translated from ICD-9 codes for carotid revascularization, and 3 codes incorrectly translated for endovascular aortic aneurysm repair.

Conclusions Algorithms to crosswalk lists of ICD-9 codes to ICD-10 codes can leverage electronic resources to minimize the burden of code translation. However, manual review for code validation may be necessary, with collaboration across institutions for researchers to share their efforts.

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Cardiac Glucolipotoxicity and Cardiovascular Outcomes.

Cardiac insulin signaling can be impaired due to the altered fatty acid metabolism to induce insulin resistance. In diabetes and insulin resistance, the metabolic, structural and ultimately functional alterations in the heart and vasculature culminate in diabetic cardiomyopathy, coronary artery disease, ischemia and eventually heart failure. Glucolipotoxicity describes the combined, often synergistic, adverse effects of elevated glucose and free fatty acid concentrations on heart structure, function, and survival. The quality of fatty acid shapes the cardiac structure and function, often influencing survival. A healthy fatty acid balance is therefore critical for maintaining cardiac integrity and function.

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Effects of intensive interventions compared to standard care in people with type 2 diabetes and microalbuminuria on risk factors control and cardiovascular outcomes: A systematic review and meta-analysis of randomised controlled trials.

Usman M, Gillies CL, Khunti K, Davies MJ

AIMS: The effect of intensive glycaemic control, blood pressure control and lipid levels control alone or as part of a multifactorial intervention has not been fully evaluated. We aimed to estimate the effects of more intensive interventions, compared with standard care, on risk factor control and cardiovascular outcomes in people with type 2 diabetes and microalbuminuria.
METHODS: We searched MEDLINE, Embase and the Cochrane library without language restrictions from inception to August 10, 2018. We included randomised controlled trials that evaluated intensive interventions in adults with type 2 diabetes and microalbuminuria. The review was registered on PROSPERO (registration number 42017055208). We used random effects meta-analysis to calculate overall pooled effect estimates across studies.
RESULTS: A total of seven (n = 1210) randomised controlled trials were included, four studies (n = 758) reported HbA1c, six studies (n = 950) reported blood pressure measurements, and three studies (n = 896) examined non-fatal MI, non-fatal stroke, cardiovascular mortality, and all-cause mortality. Intensive interventions indicated statistically significant reductions in both systolic and diastolic blood pressure, and a nonsignificant trend for reduction in HbA1c, total cholesterol, LDL, triglycerides and urinary albumin excretion rate. There was no evidence to suggest that compared with standard care, intensive interventions reduced the risk of non-fatal MI [risk ratio (RR) 0·50; 95% CI 0·20, 1·22; P = 0·127], non-fatal stroke (RR 0·44; 95% CI 0·10, 1·91; P = 0·275), CV mortality (RR 0·95; 95% CI 0·48, 1·86; P = 0·874) or all-cause mortality (RR 0·80; 95% CI 0·51, 1·25; P = 0·324).
CONCLUSIONS: Apart from blood pressure outcomes, there was no evidence that intensive interventions improve or worsen HbA1c, total cholesterol, LDL, triglycerides, urinary albumin excretion rate, risk of cardiovascular or mortality outcomes in people with type 2 diabetes and microalbuminuria. Results of this review are mainly influenced by one small trial, hence uncertainty surrounding the effect of intensive interventions in people with type 2 diabetes and microalbuminuria still exists. Large studies are urgently required in this high risk cardiovascular group of patients.

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Cardiovascular Outcomes After Lower Extremity Endovascular or Surgical Revascularization: The EUCLID Trial.

Baumgartner I, Norgren L, Fowkes FGR, Mulder H, Patel MR, Berger JS, Jones WS, Rockhold FW, Katona BG, Mahaffey K, Hiatt WR; Executive Committee and Investigators of the EUCLID Trial.

BACKGROUND: Lower extremity revascularization (LER) is a common treatment in patients with peripheral artery disease (PAD), but long-term outcomes are poorly defined.
OBJECTIVES: The aim was to analyze LER in the EUCLID (Examining Use of tiCagreLor In paD) trial to determine predictors and cardiovascular outcomes.
METHODS: Patients were grouped according to whether they received a post-randomization LER (n = 1,738) or not (n = 12,147). All variables were assessed for significance in univariable and parsimonious multivariable models. The primary endpoint was myocardial infarction, ischemic stroke, or cardiovascular death; major adverse limb events (MALE) included acute limb ischemia or major amputation.
RESULTS: A post-randomization LER occurred in 12.5% of patients and was an endovascular LER in 74.7%. Endovascular LERs were performed more often in North America, whereas surgical procedures occurred more frequently in Europe. Independent factors predicting LER were prior and type of prior LER, geographic region, limb symptoms, diabetes, and smoking. A post-randomization LER was associated with an increased risk for the primary endpoint (hazard ratio: 1.60; 95% confidence interval: 1.35 to 1.90; $p < 0.0001$) and MALE (hazard ratio: 12.0; 95% confidence interval: 9.47 to 15.30; $p < 0.0001$). Event rates for the primary endpoint after LER were numerically higher in the surgical subgroup, but MALE were similar between surgical and endovascular LER.
CONCLUSIONS: In the EUCLID trial, LER was most often endovascular. Following LER, there was an increased hazard for the primary endpoint (with higher event rates in the surgical group) and a markedly increased risk for MALE events (with similar event rates between surgical and endovascular LER procedures). (A Study Comparing Cardiovascular Effects of Ticagrelor and Clopidogrel in Patients With Peripheral Artery Disease [EUCLID]; NCT01732822).

PMID: 30261955

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Patient Diversity and Population Health-Related Cardiovascular Outcomes Associated with Warfarin Use in Atrial Fibrillation: An Analysis Using Administrative Claims Data.

Kim MH, Xu L, Puckrein G.

INTRODUCTION: Anticoagulants are effective for stroke prevention in atrial fibrillation (AF). Data on population health-related cardiovascular outcomes by race/ethnicity and gender are not well described. The aim was to assess the impact of patient diversity on associated cardiovascular outcomes related to warfarin anticoagulation in Medicare beneficiaries with AF.
METHODS: Medicare administrative claims data for years 2000-2010 were used to calculate AF prevalence and rates of new AF cases. Three 20% sample cohorts of new AF beneficiaries for years 2000, 2005, and 2007 were extracted and analyzed in a longitudinal study design. The impact of warfarin on associated cardiovascular outcomes was measured with respect to race/ethnicity and gender. Measured outcomes included the risk of stroke, mortality and hospitalization after adjusting for age, gender, race/ethnicity, CHADS2 score and warfarin.
RESULTS: AF prevalence and warfarin use increased while stroke and mortality rates declined across race/ethnicity and gender from 2000 to 2010. Analyses comparing Whites to non-Whites highlighted several disparities: (1) Blacks were 40% ($p<0.0001$) more likely to have a stroke even after adjustment for warfarin; (2) in 2007, Hispanics had a 35% ($p<0.01$) higher prevalence of stroke and warfarin did not reduce the risk; and (3) Asians had better outcomes. Warfarin reduced stroke less well in women who had a lower risk of death and hospitalization. Despite a >70% ($p<0.0001$) reduction in mortality for warfarin users, Blacks had a 25% ($p<0.0001$) higher mortality risk than Whites.
CONCLUSIONS: Differences in population health metrics across race/ethnicity and gender exist in AF. Across all metrics, Blacks had comparatively worse outcomes. Patient diversity should be a focus for future investigations in AF to improve outcomes in the whole population.
FUNDING: National Minority Quality Forum.

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Lipid lowering drugs and inflammatory changes: an impact on cardiovascular outcomes?

Ruscica M, Ferri N, Macchi C, Corsini A, Sirtori CR.

Inflammatory changes are responsible for maintenance of the atherosclerotic process and may underlie some of the most feared vascular complications. Among the multiple mechanisms of inflammation, the arterial deposition of lipids and particularly of cholesterol crystals is the one responsible for the activation of inflammasome NLRP3, followed by the rise of circulating markers, mainly C-reactive protein (CRP). Elevation of lipoproteins, LDL but also VLDL and remnants, associates with increased inflammatory changes and coronary risk. Lipid lowering medications can reduce cholesterolemia and CRP: patients with elevations of both are at greatest cardiovascular (CV) risk and receive maximum benefit from therapy. Evaluation of the major drug series indicates that statins exert the largest LDL and CRP reduction, accompanied by reduced CV events. Other drugs, mainly active on the triglyceride/HDL axis, for example, PPAR agonists, may improve CRP and the lipid pattern, especially in patients with metabolic syndrome. PCSK9 antagonists, the newest most potent medications, do not induce significant changes in inflammatory markers, but patients with the highest baseline CRP levels show the best CV risk reduction. Parallel evaluation of lipids and inflammatory changes clearly indicates a significant link, both guiding to patients at highest risk, and to the best pharmacological approach. Key messages Lipid lowering agents with "pleiotropic" effects provide a more effective approach to CV prevention In CANTOS study, patients achieving on-treatment hsCRP concentrations ≤2 mg/L had a higher benefit in terms of reduction in major CV events The anti-inflammatory activity of PCSK9 antagonists appears to be of a minimal extent.

PMID: 29976096

Diabetes Obes Metab. 2018 Oct;20(10):2379-2388

Sex differences in management and outcomes of patients with type 2 diabetes and cardiovascular disease: A report from TECOS.

Alfredsson J, Green JB(1), Stevens SR, Reed SD, Armstrong PW, Angelyn Bethel M, Engel SS, McGuire DK, Van de Werf F, Hramiak I, White HD, Peterson ED, Holman RR; TECOS Study Group.

AIM: To examine sex differences in baseline characteristics and outcomes in patients with type 2 diabetes and atherosclerotic vascular disease.
MATERIALS AND METHODS: Cox models were used to analyse the association between sex and outcomes in the Trial Evaluating Cardiovascular Outcomes with Sitagliptin (TECOS), a randomized, placebo-controlled trial assessing the impact of sitagliptin on cardiovascular (CV) outcomes in patients with type 2 diabetes and atherosclerotic vascular disease.
RESULTS: A total of 4297 women and 10 374 men were followed for a median of 3.0 years. Women were slightly older and more often had cerebrovascular disease and peripheral arterial disease but less often coronary heart disease than men. At baseline, women were less likely to use aspirin or statins. The primary composite outcome of CV death, myocardial infarction, stroke, or hospitalization for unstable angina occurred in 418 women (9.7%) and 1272 men (12.3%; 3.48 vs 4.38 events/100 participant-years, crude hazard ratio [HR] 0.79, 95% confidence interval [CI] 0.71-0.89, adjusted HR 0.64, 95% CI 0.55-0.74; P < .0001). Women also had a significantly lower risk of secondary CV outcomes and all-cause death.
CONCLUSIONS: In this large prospective study of people with type 2 diabetes and CV disease, women had different CV disease burden, worse CV risk factor profiles, and less use of indicated medications than men. Despite this, women had significantly lower risk of CV events, suggesting that the cardioprotective effects of female sex extend to populations with type 2 diabetes.

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Rationale and Methodology of the SARAH Trial: Long-Term Cardiovascular Outcomes in Patients With Resistant Hypertension and Obstructive Sleep Apnea.

[Article in English, Spanish]

Sapiña-Beltrán E, Torres G, Martínez-Alonso M, Sánchez-de-la-Torre M, Franch M, Bravo C, Masa JF, Felez M, Fortuna-Gutierrez AM, Abad J, García-Río F, Drager LF, Lee Chi-Hang R), Martínez-García MÁ), Barbé F, Dalmases M.

INTRODUCTION: Patients with resistant hypertension (RH) have a high risk of developing cardiovascular events; therefore, new therapeutic approaches to better control blood pressure may be useful in improving cardiovascular outcomes. The prevalence of obstructive sleep apnea (OSA) is very high among patients with RH. Continuous positive airway pressure (CPAP) has been shown to be an effective treatment for reducing blood pressure in patients with RH. Nevertheless, the long-term effect of CPAP treatment on cardiovascular outcomes has not been explored. The main objective of the SARAH study is to assess the impact of OSA and its treatment on cardiovascular outcomes (morbidity and mortality) in patients with RH.
METHODS: This study is a multi-center, prospective, observational cohort study. A total of 1371 patients with RH will be enrolled in the study and followed once a year for five years. At inclusion, ambulatory blood pressure monitoring (ABPM) and a sleep study will be performed in all subjects. Socio-demographic, clinical and cardiovascular variables will be collected at baseline and follow-up. Subsequently, subjects with OSA will be managed according to local standard practice. Based on the OSA diagnosis and its treatment, three cohorts of subjects with RH will be defined: non-OSA, treated OSA and non-treated OSA.
CONCLUSIONS: This study will contribute to elucidating the long-term impact of OSA treatments on blood pressure control and cardiovascular outcomes in patients with RH. These results will contribute to improve the cardiovascular prognosis of patients with RH.

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Clinical characteristics and cardiovascular outcomes in patients with atrial fibrillation receiving rhythm-control therapy: the Fushimi AF Registry.

An Y, Esato M, Ishii M, Iguchi M, Masunaga N, Tsuji H, Wada H, Hasegawa K, Ogawa H, Abe M, Lip GYH, Akao M.

Management of atrial fibrillation (AF) with current rhythm-control therapy has an uncertain impact on outcomes. Among 3731 patients in the Fushimi AF Registry, a community-based prospective survey of AF patients in Fushimi-ku, Kyoto, we investigated the characteristics and outcomes in 478 patients receiving rhythm-control therapy (anti-arrhythmic drug and/or catheter ablation) alone, with 1279 patients receiving rate-control therapy (beta-blockers, calcium channel blockers, and digoxin) alone serving as a reference. The Rhythm-control group, 26% of which had prior catheter ablation, was younger (70.5±10.8 vs. 74.3±10.4 years, P<0.001) with lower CHA2DS2-VASc score (2.71±1.63 vs. 3.64±1.62, P<0.001) and received oral anticoagulants less frequently than the Rate-control group. During the median follow-up of 1107 days, the incidence of the composite of cardiac death and heart failure (HF) hospitalization was lower with rhythm control (hazard ratio (HR) 0.24, 95% confidence interval (CI) 0.14-0.36; P<0.001), whereas that of ischemic stroke/systemic embolism was not significantly different (HR 0.64, 95% CI 0.35-1.10; P=0.12), when compared to rate control. Propensity score-matching analysis as well as multivariate analysis further supported the relation of Rhythm-control group to the lower incidence of the composite of cardiac death and HF hospitalization. Rhythm-control therapy by anti-arrhythmic drug and/or catheter ablation in the contemporary clinical practice was associated with the lower incidence of the composite of cardiac death and HF hospitalization, as compared with rate-control therapy in a Japanese AF cohort. However, given the fundamental differences in baseline clinical characteristics between the rhythm- and Rate-control groups, the results cannot be generalizable.

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