

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

# SERVIÇO DE INFORMAÇÃO CIENTÍFICA



A informação ao serviço da saúde

## Risco Cardiovascular Outcomes Cardiovasculares

2019 - nº 2

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## Índice

RISCO CARDIOVASCULAR .....	4
Associations of self-reported stair climbing with all-cause and cardiovascular mortality: The Harvard Alumni Health Study.....	5
The prevalence of cardiovascular disease and antidiabetes treatment characteristics among a large type 2 diabetes population in the United States. ....	6
Karma of Cardiovascular Disease Risk Factors for Prevention and Management of Major Cardiovascular Events in the Context of Acute Exacerbations of Chronic Obstructive Pulmonary Disease. ....	7
Benefits of the Mediterranean diet: Epidemiological and molecular aspects.....	8
Periodontal disease, smoking, cardiovascular complications and mortality in type 1 diabetes. .	9
Association Between Reported Long Working Hours and History of Stroke in the CONSTANCES Cohort.....	10
Early life socioeconomic position and mortality from cardiovascular diseases: an application of causal mediation analysis in the Stockholm Public Health Cohort. ....	11
Trends of case-fatality rate by acute coronary syndrome in Portugal: Impact of a fast track to the coronary unit.....	12
Fighting obesity in children from European World Health Organization member states. Epidemiological data, medical-social aspects, and prevention programs. ....	13
Global Impact of Peripheral Obstructive Arterial Disease in Portugal: An Eight Year Study. ....	14
[Epidemiology of hypertension: Differences between women and men].....	16
Sex difference: an important issue to consider in epidemiological and clinical studies dealing with serum paraoxonase-1. ....	17
Epidemiology, risk factors, and opportunities for prevention of cardiovascular disease in individuals of South Asian ethnicity living in Europe. ....	18
Demographic, health behavior, and cardiometabolic risk factor profile in yoga and non-yoga participants: NHANES 1999-2006. ....	19
2019 Recommendations for reducing tobacco consumption in the Portuguese-speaking countries.....	20
Temporal Trends in Ischemic Stroke Incidence in Younger Adults in the Framingham Study. ..	21
Will undocumented migrants contribute to change epidemiology, presentation and pharmacologic treatment of diabetes in Western countries?.....	22
The burden of chronic kidney disease in systemic lupus erythematosus: A nationwide epidemiologic study. ....	23

Cardiovascular disease in the kidney transplant recipient: epidemiology, diagnosis and management strategies. ....	24
[Temporal variation of Chronic Kidney Disease's epidemiology]. ....	25
Hypoglycaemia, cardiovascular disease, and mortality in diabetes: epidemiology, pathogenesis, and management. ....	26
Risk factors for cardiovascular mortality in patients with colorectal cancer: a population-based study. ....	27
Cardiovascular Effects of Drugs Used to Treat Attention-Deficit/Hyperactivity Disorder: Part 1: Epidemiology, Pharmacology, and Impact on Hemodynamics and Ventricular Repolarization. ....	28
Dietary Vitamin B6 Intake Associated with a Decreased Risk of Cardiovascular Disease: A Prospective Cohort Study. ....	30
Prevalence of Cardiovascular Risk Factors Among Cancer Patients in the United States. ....	31
A Vascular Aging Index as Independent Predictor of Cardiovascular Events and Total Mortality in an Elderly Urban Population. ....	32
Risk of cardiovascular disease outcomes in primary care subjects with familial hypercholesterolaemia: A cohort study. ....	33
Racial and ethnic differences in cardiovascular disease and outcome in type 1 diabetes patients. ....	34
Is depression a real risk factor for acute myocardial infarction mortality? A retrospective cohort study. ....	35
Low-Carbohydrate Diets and Risk of Incident Atrial Fibrillation: A Prospective Cohort Study... ..	36
Association of Low Fasting Glucose and HbA1c With Cardiovascular Disease and Mortality: The MESA Study. ....	37
Association between prediabetes (defined by HbA1C, fasting plasma glucose, and impaired glucose tolerance) and the development of chronic kidney disease: a 9-year prospective cohort study. ....	38
Population susceptibility differences and effects of air pollution on cardiovascular mortality: epidemiological evidence from a time-series study. ....	39
Cardiovascular health and sleep disturbances in two population-based cohort studies. ....	40
OUTCOMES CARDIOVASCULARES .....	41
Relation of Vegetarian Dietary Patterns With Major Cardiovascular Outcomes: A Systematic Review and Meta-Analysis of Prospective Cohort Studies. ....	42
Upstroke time per cardiac cycle is associated with cardiovascular prognosis in type 2 diabetes. ....	43
Impact of Lunar Phase on Outcomes Following ST-Elevation Myocardial Infarction. ....	44
Vitamin D Supplementation and Cardiovascular Disease Risks in More Than 83 000 Individuals in 21 Randomized Clinical Trials: A Meta-analysis. ....	45

A whole-food, plant-based nutrition program: Evaluation of cardiovascular outcomes and exploration of food choices determinants.....	46
Associations of Gout and Baseline Serum Urate Level With Cardiovascular Outcomes: Analysis of the Coronary Disease Cohort Study.....	47
Aspirin has potential benefits for primary prevention of cardiovascular outcomes in diabetes: updated literature-based and individual participant data meta-analyses of randomized controlled trials. ....	48
Assessment of Heart Failure in Diabetes Cardiovascular Outcomes Trials: Is What We Are Currently Capturing Adequate? .....	49
Risk assessment of energy drinks with focus on cardiovascular parameters and energy drink consumption in Europe.....	50
Low-density lipoprotein cholesterol lowering for the prevention of cardiovascular outcomes in patients with ischemic stroke. ....	51
Milk and Dairy Product Consumption and Cardiovascular Diseases: An Overview of Systematic Reviews and Meta-Analyses.....	52
BMI, Mortality, and Cardiovascular Outcomes in Type 1 Diabetes: Findings Against an Obesity Paradox.....	53
Glucose-lowering therapy and cardiovascular outcomes in patients with type 2 diabetes mellitus and acute coronary syndrome. ....	54
Effect of ischemic preconditioning on cardiovascular outcomes in patients with symptomatic coronary artery disease: a cohort study. ....	55
Neck circumference and cardiovascular outcomes: Insights from the Jackson Heart Study. ....	56
Albuminuria as a Predictor of Cardiovascular Outcomes in Patients With Acute Myocardial Infarction.....	57



## Risco Cardiovascular

Pesquisa Bibliográfica efectuada em Pubmed ([www.ncbi.nlm.nih.gov/](http://www.ncbi.nlm.nih.gov/)) -Abr a Jun 2019

## **Associations of self-reported stair climbing with all-cause and cardiovascular mortality: The Harvard Alumni Health Study.**

Rey-Lopez JP, Stamatakis E, Mackey M, Sesso HD, Lee IM.

To evaluate the association between numbers of floors climbed (per week) and all-cause and cardiovascular (CVD) mortality in men. A prospective study was conducted in 8874 men (Median [interquartile range] age: 65 years [60-71.6 years]) from the Harvard Alumni Health Study. Participants reported the number of floors habitually climbed, physical activity in their leisure time, other health related behaviours and any physician diagnosed disease in 1988. Men were followed for mortality through December 2008. Multivariate Cox hazard models to examine the association between weekly number of floors climbed and all-cause and CVD mortality adjusted for participation in total physical activity and other confounders. During a median follow-up of 12.4 years, 4063 men died (1195 from CVD). After adjusting for confounders (age, walking, sports/recreation, body mass index, alcohol intake, and smoking, diagnoses of hypertension or diabetes or high cholesterol) number of stairs habitually climbed was inversely associated with all-cause mortality (p trend <0.001). Compared with the group who climbed <10 floors/week, the hazard ratio (HR) for the  $\geq 35$  floors/week group was 0.84 95% confidence interval (CI) (0.78-0.91). In contrast, we found no evidence for an association between stair climbing and CVD mortality risk (p trend = 0.38), in the  $\geq 35$  floors/week group: HR = 0.94 95%CI (0.81-1.09). In this cohort of older men, stair climbing was associated with a lower risk of mortality from any causes. Further insights may be gained from future observational studies utilizing emerging pattern recognition of stair climbing from objective measurements of physical activity.

PMID: 31338282

## **The prevalence of cardiovascular disease and antidiabetes treatment characteristics among a large type 2 diabetes population in the United States.**

Weng W, Tian Y, Kong SX, Ganguly R, Hersloev M, Brett J, Hobbs T.

**Objectives:** The purpose of this study was to assess atherosclerotic cardiovascular disease (ASCVD) prevalence, antidiabetes medication usage and physician specialty encounters among individuals with type 2 diabetes mellitus (T2DM) in the United States during 2015.

**Design:** Retrospective, cross-sectional analysis.

**Patients:** Adults with T2DM in a large US administrative claims database. Patients were divided into ASCVD and non-ASCVD groups. Subgroup analyses were conducted for three age groups (18-44, 45-64 and 65+ years).

**Results:** Of 1 202 596 patients with T2DM, 45.2% had established ASCVD. About 40% of T2DM patients with ASCVD had visited a cardiologist during 2015, compared to 11% in the non-ASCVD group. The use of glucagon-like peptide-1 receptor agonists (GLP-1RAs) and sodium-glucose co-transporter 2 inhibitors (SGLT-2is) was low overall (<12%), and even lower in the ASCVD group (<9%). The prevalence of ASCVD was 15%, 36% and 71% in the 18-44, 45-64 and 65+ year age groups, respectively. GLP-1RA and SGLT-2i use was ≤5% in the 65+ subgroup, regardless of ASCVD status.

**Conclusions:** These real-world data showed a high prevalence of ASCVD among T2DM patients, and confirmed, as a baseline assessment, low use of GLP-1RAs and SGLT-2is in these at-risk patients prior to the 2017 American Diabetes Association guidelines recommending use of agents with proven cardiovascular benefits.

PMID: 31294089

## **Karma of Cardiovascular Disease Risk Factors for Prevention and Management of Major Cardiovascular Events in the Context of Acute Exacerbations of Chronic Obstructive Pulmonary Disease.**

Crisan L, Wong N, Sin DD, Lee HM

There is compelling epidemiological evidence that airway exposure to cigarette smoke, air pollution particles, as well as bacterial and viral pathogens is strongly related to acute ischemic events. Over the years, there have been important animal and human studies that have provided experimental evidence to support a causal link. Studies show that patients with cardiovascular diseases (CVDs) or risk factors for CVD are more likely to have major adverse cardiovascular events (MACEs) after an acute exacerbation of chronic obstructive pulmonary disease (COPD), and patients with more severe COPD have higher cardiovascular mortality and morbidity than those with less severe COPD. The risk of MACEs in acute exacerbation of COPD is determined by the complex interactions between genetics, behavioral, metabolic, infectious, and environmental risk factors. To date, there are no guidelines regarding the prevention, screening, and management of the modifiable risk factors for MACEs in the context of COPD or COPD exacerbations, and there is insufficient CVD risk control in those with COPD. A deeper insight of the modifiable risk factors shared by CVD, COPD, and acute exacerbations of COPD may improve the strategies for reduction of MACEs in patients with COPD through vaccination, tight control of traditional CV risk factors and modifying lifestyle. This review summarizes the most recent studies regarding the pathophysiology and epidemiology of modifiable risk factors shared by CVD, COPD, and COPD exacerbations that could influence overall morbidity and mortality due to MACEs in patients with acute exacerbations of COPD.

PMID: 31294030



## **Benefits of the Mediterranean diet: Epidemiological and molecular aspects.**

Serra-Majem L, Román-Viñas B, Sanchez-Villegas A, Guasch-Ferré M, Corella D, La Vecchia C

More than 50 years after the Seven Countries Study, a large number of epidemiological studies have explored the relationship between the Mediterranean diet (MD) and health, through observational, case-control, some longitudinal and a few experimental studies. The overall results show strong evidence suggesting a protective effect of the MD mainly on the risk of cardiovascular disease (CVD) and certain types of cancer. The beneficial effects have been attributed to the types of food consumed, total dietary pattern, components in the food, cooking techniques, eating behaviors and lifestyle behaviors, among others. The aim of this article is to review and summarize the knowledge derived from the literature focusing on the benefits of the MD on health, including those that have been extensively investigated (CVD, cancer) along with more recent issues such as mental health, immunity, quality of life, etc. The review begins with a brief description of the MD and its components. Then we present a review of studies evaluating metabolic biomarkers and genotypes in relation to the MD. Other sections are dedicated to observation and intervention studies for various pathologies. Finally, some insights into the relationship between the MD and sustainability are explored. In conclusion, the research undertaken on metabolomics approaches has identified potential markers for certain MD components and patterns, but more investigation is needed to obtain valid measures. Further evaluation of gene-MD interactions are also required to better understand the mechanisms by which the MD diet exerts its beneficial effects on health. Observation and intervention studies, particularly PREDIMED, have provided invaluable data on the benefits of the MD for a wide range of chronic diseases. However further research is needed to explore the effects of other lifestyle components associated with Mediterranean populations, its environmental impact, as well as the MD extrapolation to non-Mediterranean contexts.

PMID: 31254553

## **Periodontal disease, smoking, cardiovascular complications and mortality in type 1 diabetes.**

Khouja T, Miller RG, Moore PA, Orchard TJ, Costacou T.

**AIM:** To assess the role of periodontal disease (PD) as a predictor of coronary artery disease (CAD) and mortality in a prospective type 1 diabetes (T1D) cohort and to evaluate the role of smoking in this relationship.

**METHODS:** Data were based on 320 participants of the Pittsburgh Epidemiology of Diabetes Complications study of T1D who, during 1992-94, received a partial mouth periodontal exam, and who were followed for up to 19 years to ascertain complication incidence. PD was defined as clinical attachment loss of  $\geq 4$  mm for at least 10% of the examined sites. Predictors of all-cause mortality; Hard CAD (CAD death, myocardial infarction or revascularization), and Total CAD (Hard CAD, angina, ischemic ECG) were assessed using Cox models.

**RESULTS:** During 19 years of follow-up, 33.7% (97/288) developed CAD, 27.3% (83/304) developed Hard CAD, and 16.9% (54/320) died. Among current smokers, 46.4% (26/56) developed CAD, 42.7% (24/56) developed Hard CAD and 29.5% (18/61) died. PD was not associated with all-cause mortality, although it was a significant predictor of both CAD (HR = 1.12, CI = 1.01-1.23) and Hard CAD (HR = 1.30, CI = 1.11-1.51). As smoking modified the PD-CAD and PD-Hard CAD associations, analyses were stratified by smoking status. PD was associated with an increased risk of CAD (HR = 1.25, CI = 1.03-1.50) and Hard CAD (HR = 1.85, CI = 1.17-2.93) only among smokers.

**CONCLUSION:** PD was a significant predictor of CAD and Hard CAD among current smokers with T1D.

PMID: 31235433

## **Association Between Reported Long Working Hours and History of Stroke in the CONSTANCES Cohort.**

Fadel M, Sembajwe G, Gagliardi D Pico F, Li J, Ozguler A, Siegrist J, Evanoff BA, Baer M, Tsutsumi A, Iavicoli S, Leclerc A, Roquelaure Y, Descatha A.

**Background and Purpose-** Long working hours (LWHs) are a potential risk factor for stroke. The aim of this study was to investigate this association in a large general population cohort. **Methods-** We used the French population-based cohort, CONSTANCES (Cohorte des Consultants des Centres d'Examens de Santé), to retrieve information on age, sex, smoking, and working hours from the baseline, self-administered questionnaire. Other cardiovascular risk factors and previous occurrence of stroke were taken from a parallel medical interview. We defined LWH as working time >10 hours daily for at least 50 days per year. Participants with primarily part-time jobs were excluded as were those with stroke before LWH exposure. We used logistic models to estimate the association between LWH and stroke, stratified by age, sex, and occupation. In additional modeling, we excluded subjects whose stroke occurred within 5 years of the first reported work exposure.

**Results-** Among the 143592 participants in the analyses, there were 1224 (0.9%) strokes, 42542 (29.6%) reported LWH, and 14481 (10.1%) reported LWH for 10 years or more. LWH was associated with an increased risk of stroke: adjusted odds ratio of 1.29 (95% CI, 1.11-1.49). Being exposed to LWH for 10 years or more was more strongly associated with stroke, adjusted odds ratio of 1.45 (95% CI, 1.21-1.74). The association showed no differences between men and women but was stronger in white-collar workers under 50 years of age.

**Conclusions-** This large analysis reveals a significant association between stroke and exposure to LWH for 10 years or more. The findings are relevant for individual and global prevention.

PMID: 31216962

## **Early life socioeconomic position and mortality from cardiovascular diseases: an application of causal mediation analysis in the Stockholm Public Health Cohort.**

Hossin MZ, Koupil I, Falkstedt D.

**OBJECTIVE:** We aimed to quantify the mediating impact of adult social and behavioural mechanisms in the association between childhood socioeconomic position (SEP) and cardiovascular disease (CVD) mortality by employing a weighting approach to mediation analysis.

**DESIGN:** Prospective cohort study.

**SETTING:** Stockholm County, Sweden.

**PARTICIPANTS:** 19 720 individuals who participated in the Stockholm Public Health Cohort survey in 2002 and were older than 40 years.

**PRIMARY AND SECONDARY OUTCOME MEASURES:** The primary outcome was CVD mortality. Non-CVD mortality was additionally analysed for comparison.

**METHODS:** Study subjects were followed in routine registers from 2002 to 2011 for mortality. Data on father's SEP and adult social and behavioural factors came from questionnaire survey. The inverse odds weighting method was used to estimate the total effect, the natural direct effect and the natural indirect effect (NIE) in Poisson regression models. All results were adjusted for gender, age, country of birth and marital status. Multiple imputation was used to handle missing data.

**RESULTS:** The total effect of manual versus non-manual father's SEP on CVD mortality was estimated as an incidence rate ratio (IRR) of 1.24 (95% CI 1.09 to 1.41). When the social and behavioural factors were accounted for, the IRR for the NIE was 1.09 (95% CI 1.04 to 1.14), suggesting a mediation of 44% of the total effect. As for non-CVD mortality, father's manual SEP was associated with 1.15 fold excess risk (IRR: 1.15; 95% CI 1.04 to 1.27) of which the effect represented by the whole set of mediators was 1.06 (95% CI 1.01 to 1.10).

**CONCLUSION:** Adult social and behavioural factors had a considerable mediating effect on the early life social origin of mortality from CVDs and other causes. Future research employing causal mediation analysis may nevertheless have to consider additional factors for a fuller understanding of the mechanisms.

PMID: 31209086

## **Trends of case-fatality rate by acute coronary syndrome in Portugal: Impact of a fast track to the coronary unit.**

Abreu D, Pinto FJ, Matias-Dias C, Sousa P.

**Introduction:** Efforts were made to improve management of coronary disease as the fast-track system to the Coronary Unit. We aim to analyse case-fatality rates by acute coronary syndrome in Portugal from 2000 to 2016, mainly the impact of the fast-track system and the proportion of patients that activate the fast-track system.

**Methods:** We analysed monthly acute coronary syndrome case-fatality before and after the implementation of the fast-track system in 2007. Impact of the system was assessed through regression models for interrupted time-series. We calculated annual proportion of fast-track system admissions.

**Results:** After 2007 case-fatality by acute coronary syndrome decreased ( $\beta=-1.27$ ,  $p$ -value  $<0.01$ ). The estimates obtained for ST Elevation Myocardial Infarction suggest a reduction of nearly 86 monthly deaths prevented after 2007. The highest percentage of patients admitted through the fast-track system was 35%.

**Conclusions:** Our results suggest fast-track system may have contributed to a decline in acute coronary syndrome case-fatality. However, more than half of patients were not admitted through the system. This should encourage health authorities to make efforts to ensure compliance.

PMID: 31205687

## **Fighting obesity in children from European World Health Organization member states. Epidemiological data, medical-social aspects, and prevention programs.**

Nittari G, Scuri S, Petrelli F, Pirillo I, di Luca NM, Grappasonni I.

Childhood obesity is one of the most serious public health challenges of this century. Overweight and obese children are likely to stay obese into adulthood and more likely to develop non-communicable diseases like diabetes and cardiovascular diseases at a younger age. In the WHO European Region one child out of 3, is overweight or obese. Over 60% of children who are overweight before puberty will be overweight in early adulthood. Children and adolescents, aged 5-19 have shown rising obesity rates in almost all nations, including where the situation was far from alarming 40 years ago. Several nations have seen the prevalence almost double: Israel has gone from 5.8% in 1975 to 11.9% in 2016, Andorra from 6.2% to 12.8%, and Malta from 7.4% to 13.4%. Analyzing overweight and obesity, we can see that they follow similar trends and patterns. In 1975 the majority of European countries had a prevalence less than 10% and obesity less than 5%, while no European country had overweight prevalence higher than 30% and obesity higher than 10%. In 2016 the trend reversed, showing a worrying increase in the number of European countries with a high prevalence of overweight (over 30%) and obesity (over 10%) (Fig. 1)(29). Starting from the analysis of epidemiological data on obesity in the WHO European Region, the paper analyzes the adopted prevention programs in order to assess their effectiveness and figure out the best strategies to reduce the prevalence of overweight and obesity. The WHO European Childhood Obesity Surveillance Initiative reported that children tend to overeat and not to do enough physical exercise. Different preventive programs have identified different areas of action and corresponding measures: consumption of healthy foods, physical exercise, care before conception and during pregnancy, early childhood, school age children, weight management, monitoring and evaluation. Primary prevention is essential to reduce obesity incidence: it is easier to act on the adoption of healthy eating habits than intervene with diets on children who already have weight issues. Working on prevention programs represents an investment for the future of children's health. By simply acting on prevention, particularly on body weight reduction, it could be possible to tackle the spreading of correlated diseases. Therefore, prevention programs ought to be prioritized priority at a national and international level.

PMID: 31173054 [Indexed for MEDLINE]

## **Global Impact of Peripheral Obstructive Arterial Disease in Portugal: An Eight Year Study.**

Moutinho M, Simões I, Rodrigues S, Abreu D, Silva E, Sousa P, Fernandes JF.

**INTRODUCTION:** Peripheral arterial disease has an important impact on morbidity/mortality. The objective of this study was to quantify the impact of this disease in Portugal during the last eight years, expressed by the volume of admissions, treatment strategies and associated morbidity and mortality.

**MATERIAL AND METHODS:** We collected data from the Diagnosis Related Group national database on primary diagnosis, procedures codes, demographic variables, a number of risk factors, and mortality of all cases admitted from 2009 to 2016 with a primary diagnosis of peripheral arterial disease coded according to the 9<sup>th</sup> revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-9).

**RESULTS:** In this study, peripheral arterial disease led to 27 684 hospitalisations, which corresponded to 26.7% of all admissions for vascular disease in this period. Approximately 49.9% of patients were admitted to the emergency department. The volume of procedures in patients with claudication decreased over the eight years, unlike patients with critical ischaemia, in which the number of procedures increased.

**DISCUSSION:** Age and the presence of cardiovascular risk factors have been associated with the severity of disease, as observed in our series. Overall hospital mortality varied, being significantly higher in patients with more advanced severity of the disease.

**CONCLUSION:** Peripheral arterial disease represents an important burden in the overall volume of admissions in Portuguese public hospitals. A large number of patients was admitted in the context of emergency.

**Publisher:**

**Introdução:** A doença arterial obstrutiva periférica tem um importante impacto a nível de morbi/mortalidade. O objetivo deste trabalho é quantificar o impacto desta doença em Portugal, ao longo dos últimos oito anos, expresso pelo volume de internamento, tratamento e pela morbi-mortalidade respetiva.

**Material e Métodos:** Foram analisados os registos de internamento no Serviço Nacional de Saúde entre 2009 e 2016 da base de dados dos grupos de diagnósticos homogéneos utilizando os códigos 9th revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-9) de diagnóstico e procedimentos. Verificámos o número de casos em cada ano por estadio de doença, dados demográficos, fatores de risco, tratamento e morbi-mortalidade.

Resultados: No período de estudo a doença arterial periférica conduziu a 27 684 internamentos o que correspondeu a cerca de 26,7 % do total de internamentos por patologia vascular neste período. Cerca de 49,9 % dos doentes foram admitidos em contexto de urgência. Os procedimentos em doentes claudicantes diminuíram ao longo dos oito anos ao contrário dos doentes com isquemia crítica em que os procedimentos aumentaram.

Discussão: A idade e a presença de fatores de risco cardiovasculares têm sido associadas à gravidade da doença, tal como na nossa série. A mortalidade hospitalar global varia, sendo mais significativa nos doentes com doença mais avançada.

Conclusão: A doença arterial periférica é uma patologia com importante representação no internamento dos hospitais do Serviço Nacional de Saúde. Há ainda um importante volume de doentes admitidos no contexto de urgência o que sugere eventual falta de reconhecimento/referenciação atempada por parte dos cuidados saúde primários, devendo mais esforços ser realizados no sentido de aumentar a interação entre os cuidados de saúde primários e os hospitais terciários.

PMID: 31166895



## **[Epidemiology of hypertension: Differences between women and men].**

[Article in French]

Blacher J, Kretz S, Sorbets E, Lelong H, Vallée A, Lopez-Sublet M.

### PREVALENCE OF HYPERTENSION LESS FREQUENT IN WOMEN BEFORE MENOPAUSE:

In adults, up to the age of 50-60, hypertension is an uncommon disease, less frequent in women than in men. The literature review does not determine whether this difference is related to a protective effect of endogenous estrogens on the risk of high blood pressure, to genetic or immuno-enzymatic differences related to sex but of non-hormonal origin or to a large number of confounding variables (salt consumption, alcohol consumption, fruit and vegetable consumption, body mass index, psycho-socio-economic factors, sedentary lifestyle).

### PREVALENCE OF HYPERTENSION INCREASES AT MENOPAUSE:

After menopause, the risk of hypertension in women increases and quickly reaches that of men, even exceeding it from the seventh decade onwards. The factors that make hypertension more frequent after the seventh decade in women are related to differences in cardiovascular risk and life expectancy between men and women, as well as a likely surviving effect in older men. The mechanisms by which estrogen-progestin deficiency increases the risk of hypertension have been extensively studied. These mechanisms are obviously numerous. However, it has not been clearly demonstrated that hormone replacement therapy during menopause reduces blood pressure levels. It should be noted that the route of administration, the choice of molecules, the respect of the intervention window and the dosage seem to modulate the potential vascular effects.

PMID: 31151845

## **Sex difference: an important issue to consider in epidemiological and clinical studies dealing with serum paraoxonase-1.**

Trentini A, Bellini T, Bonaccorsi G, Cavicchio C, Hanau S, Passaro A, Cervellati C.

The aim of this study was to evaluate the influence of sex on serum paraoxonase-1 (PON1) activities and on its relationship with cardiovascular disease risk factors such as overall and central obesity. Arylesterase and lactonase activities of PON1 were assessed in 374 women and 92 men. Both arylesterase and lactonase activities were significantly higher in women compared to men ( $p < 0.001$ ), irrespectively of confounders such as high density lipoprotein-cholesterol, age, smoking and body mass index or waist circumference. Sex also strongly influenced the interplay between PON1 and both fat measures, with only the arylesterase showing a significant and independent inverse correlation with the former parameter ( $r = -0.248$ ,  $p < 0.001$ ) and the risk of overall obesity (odds ratio: 0.559, 95% confidence interval: 0.340-0.919) in women, but not in men; conversely, neither of the two activities remained associated with waist circumference in men or women after full adjustment. Noteworthy, the association between arylesterase and BMI in the female subsample was significant among women younger than forty-five years ( $r = -0.453$ ,  $p < 0.001$ ,  $R^2 = 0.207$ ). In conclusion, our study suggests that sex might chiefly influence PON1 activity and its contribution to cardiovascular disease risk. Further studies are needed to confirm and clarify our preliminary findings.

PMID: 31138960

## **Epidemiology, risk factors, and opportunities for prevention of cardiovascular disease in individuals of South Asian ethnicity living in Europe.**

Cainzos-Achirica M, Fedeli U, Sattar N, Agyemang C, Jenum AK, McEvoy JW, Murphy JD, Brotons C, Elosua R, Bilal U, Kanaya AM, Kandula NR, Martinez-Amezcuca P, Comin-Colet J, Pinto X.

South Asian (SA) individuals represent a large, growing population in a number of European countries. These individuals, particularly first-generation SA immigrants, are at higher risk of developing type 2 diabetes, atherogenic dyslipidaemia, and coronary heart disease than most other racial/ethnic groups living in Europe. SAs also have an increased risk of stroke compared to European-born individuals. Despite a large body of conclusive evidence, SA-specific cardiovascular health promotion and preventive interventions are currently scarce in most European countries, as well as at the European Union level. In this narrative review, we aim to increase awareness among clinicians and healthcare authorities of the public health importance of cardiovascular disease among SAs living in Europe, as well as the need for tailored interventions targeting this group - particularly, in countries where SA immigration is a recent phenomenon. To this purpose, we review key studies on the epidemiology and risk factors of cardiovascular disease in SAs living in the United Kingdom, Italy, Spain, Denmark, Norway, Sweden, and other European countries. Building on these, we discuss potential opportunities for multi-level, targeted, tailored cardiovascular prevention strategies. Because lifestyle interventions often face important cultural barriers in SAs, particularly for first-generation immigrants; we also discuss features that may help maximise the effectiveness of those interventions. Finally, we evaluate knowledge gaps, currently available risk stratification tools such as QRISK-3, and future directions in this important field.

PMID: 31128454

## **Demographic, health behavior, and cardiometabolic risk factor profile in yoga and non-yoga participants: NHANES 1999-2006.**

Forseth B, Boyer W, Miller A, Fitzhugh EC.

**OBJECTIVE:** To examine and compare the demographic, health behavior, and cardiometabolic risk factor characteristics of participants who report 1) participating in yoga, 2) not participating yoga, or 3) are inactive, using a nationally representative sample of U.S. adults.

**DESIGN:** Study participants were from the 1999-2006 National Health and Nutrition Examination Survey (NHANES) who self-reported participation in yoga (n=74), no-yoga (n=3,753) or were inactive (n=1,285). Participants in the no-yoga group did engage in other types of physical activity, while the inactive group reported no activity during the survey period.

**RESULTS:** Yoga participants were primarily female (80.7%), college educated (51.9%), mostly non-smokers (46.9%), and reported moderate alcohol consumption (72.1%). Yoga participants were found to be significantly less likely to have an elevated waist circumference (OR=0.40,  $p<0.01$ ; OR=0.30,  $p<0.01$ ), and a low HDL (OR=0.43,  $p=0.03$ ; OR=0.34,  $p<0.05$ ) compared to both non-yoga participants and inactive individuals, respectively. Yoga participants were 61% less likely to have elevated blood glucose compared to non-yoga participants (OR=0.39,  $p<0.05$ ). Compared to inactive individuals, yoga participants were 52% (OR=0.48,  $p<0.05$ ) and 66% (OR=0.34,  $p<0.05$ ) less likely have an elevated body mass index and have elevated triglyceride levels, respectively.

**CONCLUSIONS:** Given the emergence of yoga as a common form of physical activity, it is imperative to understand the characteristics of those who participate in yoga to further understand its relationship with cardiovascular risk. This study was one of the first to use nationally-representative data and objectively measured cardiometabolic variables. **Key Words:** complementary medicine, epidemiology, survey, population, physical activity, cardiovascular disease.

PMID: 31126544

## **2019 Recommendations for reducing tobacco consumption in the Portuguese-speaking countries.**

[Article in English, Portuguese]

Oliveira GMM, Mendes M, Dutra ÓP, Achutti A, Fernandes M, Correia VA, Ferreira MBSECDS, Coelho AS, Soares MBDPC, Évora MABL, Mariotto MG, Morais JCA.

After several decades of initiatives at international and national level inspired by the World Health Organization, tobacco consumption is still the second leading cause of death in the world and the leading cause of premature death and disability, as a result of various types of cancer and pulmonary, cerebrovascular and cardiovascular disease. Tobacco consumption is also an important public health issue in Portuguese-speaking countries, which fully justifies the launch and implementation of these 2019 recommendations for reducing tobacco consumption in Portuguese-speaking countries by the Federation of Portuguese Language Cardiology Societies. This position statement reviews recent changes in and the present epidemiology of tobacco consumption in the Portuguese-speaking countries, discusses the negative health impact of new forms of tobacco consumption, and addresses available prevention and drug treatment strategies. Eliminating smoking requires a coordinated effort between various national and international bodies, with a policy approach in each country focusing on laws, education campaigns for primary prevention aimed at to the general public, particularly to encourage young people not to start smoking, and a health system approach to help smokers quit smoking permanently by a combination of drug treatment and cognitive behavioral therapy. The aim is to control the only cardiovascular risk factor that can be completely eliminated. This position statement aims to alert health professionals to the need to approach the subject of smoking cessation with patients and their families during hospitalizations and outpatient consultations, and to provide them with up-to-date knowledge on how to quit smoking and maintain control of this risk factor in the long term.

PMID: 31122864

## **Temporal Trends in Ischemic Stroke Incidence in Younger Adults in the Framingham Study.**

Aparicio HJ, Himali JJ, Satizabal CL, Pase MP, Romero JR, Kase CS, Beiser AS, Seshadri S.

**Background and Purpose-** Stroke at midlife has a disproportionately large impact on disability-adjusted life-years lost. Ischemic stroke incidence may be increasing at this age. We investigated long-term trends in ischemic stroke incidence and changes in stroke risk factors in a community sample stratified by stroke onset at middle and older age.

**Methods-** In the Framingham Study, surveillance for incident stroke is ongoing since 1948. We examined age-adjusted and sex-adjusted 10-year incidence of ischemic stroke using Cox models in persons aged 35 to 54 and  $\geq 55$  years at start of follow-up. Tests for linear trend were performed over 4 epochs, controlling for the distance in time between intervals. Further, we calculated the mean 10-year risk of stroke at each epoch and for both age groups, based on vascular risk factors from the Framingham Stroke Risk Profile.

**Results-** There were 153, 197, 176, and 165 incident ischemic strokes within each epoch beginning in 1962 (n=3966), 1971 (n=5779), 1987 (n=5133), and 1998 (n=6964). Most ischemic strokes at midlife (n=71) were because of atherosclerotic brain infarction (n=50) or cardioembolism (n=19). Using the risk in the 1962 epoch as the reference, the risk of ischemic stroke at midlife did not significantly decline (hazard ratio, 0.87; 95% CI, 0.74-1.02; P trend =0.09). Incidence of ischemic stroke declined in the older group (hazard ratio, 0.82; 95% CI, 0.77-0.88; P trend <0.001). Between epochs 1 and 4, the average 10-year risk of stroke, as estimated by the Framingham Stroke Risk Profile, declined by 0.7% at midlife and 1.1% at older age.

**Conclusions-** Long-term rates of ischemic stroke declined in our community sample; the decline was greater in older as compared with younger adults. Early prevention, focused on modification of cardiovascular risk factors, is important to see sustained declines in stroke incidence and mortality at midlife.

PMID: 31084341

## **Will undocumented migrants contribute to change epidemiology, presentation and pharmacologic treatment of diabetes in Western countries?**

Fiorini G, Milani S, Pincelli AI, Calella D, Galliani S, Badalamenti S, Rigamonti AE, Marazzi N, Sartorio A, Cella SG.

**AIMS:** Migrants from countries in which health and social conditions are unsatisfactory, and their offspring, are becoming a growing component of the western population. Available health data show that their morbidity is at least comparable to that of the host country population, with a significant contribution of chronic diseases as diabetes. The possibility that diabetes shows different features in undocumented migrants is the hypothesis that we tried to investigate in this study.

**METHODS:** We retrospectively analysed the data of 413 patients with type 2 diabetes mellitus (T2DM): 222 patients followed in a diabetes clinic at a University Hospital and 191 undocumented migrants cared for by a Charity in Milan, Italy.

**RESULTS:** We found that the onset of the disease was earlier in migrants; they showed a significant lower body mass index (BMI) and had lower socioeconomic conditions. They had a worse glycaemic control. The pattern of complications was also different between the two groups, with cardiovascular complications more frequent in Italians. Finally, also pharmacologic treatment differed significantly.

**CONCLUSIONS:** Age of onset, clinical manifestations and complications of T2DM in undocumented migrants and natives may show significant differences. This is important for both epidemiological and clinical reasons. If these preliminary observations are confirmed by larger studies, we can conclude that undocumented migrants should be screened for T2DM earlier than natives, and that therapies should be tailored to the specific features of their disease.

PMID: 31064703

## **The burden of chronic kidney disease in systemic lupus erythematosus: A nationwide epidemiologic study.**

Mageau A, Timsit JF, Perrozzello A, Ruckly S, Dupuis C, Bouadma L, Papo T, Sacre K.

**OBJECTIVE:** To analyze the impact of chronic kidney disease (CKD) on major clinical outcome in SLE by using a nationwide database.

**PATIENTS AND METHODS:** Characteristics of all admitted SLE patients experiencing CKD (eGFR <60 mL/min/1.73 m<sup>2</sup>) in France from 2009 to 2015 were analyzed through the French medico- administrative database. Factors associated with CKD and major clinical outcomes such as end-stage renal disease (ESRD), cardiovascular event (CVE), septic shock and death were assessed. We used a multivariate Cox proportional hazard model and subdistribution hazard models to analyze survival without major clinical events according to the presence of CKD.

**RESULTS:** From 2009 to 2015, 26,320 SLE patients were hospitalized in France. Among them, 6439 (86.5% women; mean age 45.7 [16.5] years old) had a baseline stay in 2009 during which CKD was reported in 428 (6.7%) cases. Multivariate analysis showed that lupus nephritis (OR 6.6 [5.2-8.4]), high blood pressure (OR 3.5 [2.8-4.5]), septic shock (OR 3.2 [1.7-6.0]) and past cardiovascular history (OR 1.4 [1.0-2.0]) were associated with CKD status. From 2009 to 2015, ESRD, CVE, septic shock, and death occurred in 4.0%, 14.4%, 6.3% and 9.6% of the 6439 SLE patients. CKD at baseline was independently and strongly associated with the occurrence of ESRD (sdHR 15.9 [11.6-21.9]), CVE (sdHR 1.7 [1.4-2.2]), septic shock (sdHR 2.1 [1.5-2.8]) and death (HR 1.7 [1.3-2.2]) during the follow up.

**CONCLUSION:** CKD is a major risk factor for overall morbidity and mortality in SLE patients, highlighting the need for early pre-CKD lupus nephritis diagnosis and treatment.

PMID: 31059847 [Indexed for MEDLINE]



## **Cardiovascular disease in the kidney transplant recipient: epidemiology, diagnosis and management strategies.**

Rangaswami J, Mathew RO, Parasuraman R, Tantisattamo E, Lubetzky M, Rao S, Yaqub MS, Birdwell KA, Bennett W, Dalal P, Kapoor R, Lerma EV, Lerman M, McCormick N, Bangalore S, McCullough PA, Dadhanian DM.

Kidney transplantation (KT) is the optimal therapy for end-stage kidney disease (ESKD), resulting in significant improvement in survival as well as quality of life when compared with maintenance dialysis. The burden of cardiovascular disease (CVD) in ESKD is reduced after KT; however, it still remains the leading cause of premature patient and allograft loss, as well as a source of significant morbidity and healthcare costs. All major phenotypes of CVD including coronary artery disease, heart failure, valvular heart disease, arrhythmias and pulmonary hypertension are represented in the KT recipient population. Pre-existing risk factors for CVD in the KT recipient are amplified by superimposed cardio-metabolic derangements after transplantation such as the metabolic effects of immunosuppressive regimens, obesity, posttransplant diabetes, hypertension, dyslipidemia and allograft dysfunction. This review summarizes the major risk factors for CVD in KT recipients and describes the individual phenotypes of overt CVD in this population. It highlights gaps in the existing literature to emphasize the need for future studies in those areas and optimize cardiovascular outcomes after KT. Finally, it outlines the need for a joint 'cardio-nephrology' clinical care model to ensure continuity, multidisciplinary collaboration and implementation of best clinical practices toward reducing CVD after KT.

PMID: 30984976

## **[Temporal variation of Chronic Kidney Disease's epidemiology].**

[Article in Italian]

Provenzano M, Mancuso C, Garofalo C, De Nicola L, Andreucci M.

Chronic Kidney Disease (CKD) is a major risk factor for mortality and morbidity, as well as a growing public health problem. Several studies describe the epidemiology of CKD (i.e. prevalence, incidence) by examining short time intervals. Conversely, the trend of epidemiology over time has not been well investigated, although it may provide useful information on how to improve prevention measures and the allocation of economic resources. Our aim here is to describe the main aspects of the epidemiology of CKD by focusing on its temporal variation. The global incidence of CKD has increased by 89% in the last 27 years, primarily due to the improved socio-demographic index and life-expectancy. Prevalence has similarly increased by 87% over the same period. Mortality rate has however decreased over the last decades, both in the general and CKD populations, due to a reduction in cardiovascular and infectious disease mortality. It is important to emphasize that the upward trend of incidence and prevalence of CKD can be explained by the ageing of the population, as well as by the increase in the prevalence of comorbidities such as hypertension, diabetes and obesity. It seems hard to compare trends between Italy and other countries because of the different methods used to assess epidemiologic measures. The creation of specific CKD Registries in Italy appears therefore necessary to monitor the trend of CKD and its comorbidities over time.

PMID: 30983174

Lancet Diabetes Endocrinol. 2019 May;7(5):385-396.

## **Hypoglycaemia, cardiovascular disease, and mortality in diabetes: epidemiology, pathogenesis, and management.**

International Hypoglycaemia Study Group.

Erratum in

Lancet Diabetes Endocrinol. 2019 Jun;7(6):e18.

Hypoglycaemia has long been recognised as a dangerous side-effect of treatment of diabetes with insulin or insulin secretagogues. With its potential to disrupt cerebral function, hypoglycaemia can have a major effect on peoples' lives. Study findings have suggested that hypoglycaemia is associated with an increased risk of cardiovascular events and mortality. Different mechanisms by which hypoglycaemia might provoke cardiovascular events have been identified in experimental studies, and in clinical studies cardiac arrhythmias have been reported to be induced by hypoglycaemia, with one report describing sudden death during a severe episode. Emerging evidence suggests that the association between hypoglycaemia and cardiovascular events and mortality is likely to be multifactorial. The association is probably partly caused by confounding, with hypoglycaemia occurring more frequently in people with comorbidities who are also more likely to die than those without. However, people with type 1 or type 2 diabetes also seem at risk of hypoglycaemia-induced cardiovascular effects. This risk should be recognised by clinicians when agreeing glycaemic goals with patients and choosing appropriate glucose-lowering therapies.

PMID: 30926258

## **Risk factors for cardiovascular mortality in patients with colorectal cancer: a population-based study.**

Gaitanidis A, Spathakis M, Tsalikidis C, Alevizakos M, Tsaroucha A, Pitiakoudis M.

**BACKGROUND:** Patients with colorectal cancer are at increased risk of cardiovascular mortality compared to the general population. The purpose of this study is to identify risk factors of cardiovascular mortality in patients with colorectal cancer.

**METHODS:** A retrospective review of the Surveillance Epidemiology and End Results (SEER) database was performed between 2010 and 2014. Standardized Mortality Ratios (SMRs) for cardiovascular mortality were calculated by comparing the number of expected deaths in the United States according to the National Center for Health Statistics (ICD-10 codes I00-I99) to the number of observed deaths in the database. Logistic regression was used to identify independent risk factors.

**RESULTS:** Overall, 164,719 patients were identified (mean age at diagnosis  $67 \pm 13.9$  years, 52.7% males, 47.3% females), of which 4854 (2.9%) died from cardiovascular disease. The majority of cardiovascular deaths occurred during the first year after diagnosis (2658, 54.8%). SMRs for cardiovascular mortality were 11.7 (95% CI 11.3-12) among all patients, 12.1 (95% CI 11.7-12.6) for male patients and 11.1 (95% CI 10.6-11.6) for female patients, with SMRs being higher for younger patients. Older age, male sex, African-American race, elevated CEA and not undergoing curative surgery were independent risk factors of cardiovascular mortality in patients with colorectal cancer.

**CONCLUSION:** Patients with colorectal cancer are associated with an increased risk of cardiovascular death, especially during the first year after diagnosis. Older age, male sex, African-American race, elevated CEA and not undergoing curative surgery are independent risk factors of cardiovascular death.

PMID: 30604158 [Indexed for MEDLINE]

## **Cardiovascular Effects of Drugs Used to Treat Attention-Deficit/Hyperactivity Disorder: Part 1: Epidemiology, Pharmacology, and Impact on Hemodynamics and Ventricular Repolarization.**

Fay TB, Alpert MA

Attention-deficit/hyperactivity disorder (ADHD) is a clinical syndrome characterized by persistent inattention, impulsivity, and hyperactivity. It is most commonly encountered in children and adolescents but may persist into adulthood. A variety of psychostimulant and nonpsychostimulant medications have proven to be successful in reducing inattention, impulsivity, and hyperactivity in those with ADHD. Psychostimulants used to treat ADHD include methylphenidate and related drugs and various amphetamine preparations. Nonpsychostimulant 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 by 3-10 beats/min, systolic blood pressure by 3-8mm Hg, and diastolic blood pressure by 2-14 mm Hg. These drugs may also delay ventricular repolarization. The alpha-2 adrenergic agonists may reduce heart rate and blood pressure. For these reasons, there is concern about the safety of psychostimulant and nonpsychostimulant medications in patients with ADHD. In part 1 of this review, we discuss the epidemiology and natural history of ADHD, describe the pharmacology of drugs used to treat ADHD, and discuss in detail studies assessing the effects of ADHD drugs on blood pressure, heart or pulse rate, and electrocardiographic indices of ventricular repolarization.

PMID: 30365404 [Indexed for MEDLINE]

Am Heart J. 2019 Sep;215:70-77.

Contemporary epidemiology of infective endocarditis in patients with congenital heart disease: A UK prospective study.

Cahill TJ, Jewell PD, Denne L, Franklin RC, Frigiola A, Orchard E, Prendergast BD.

**OBJECTIVES:** Infective endocarditis is a life-threatening complication of congenital heart disease (CHD), but there are few studies concerning the contemporary risk profile, preceding invasive procedures and outcomes in this patient population. The aim of this study was to investigate the epidemiology of infective endocarditis (IE) in patients with CHD.

**METHODS:** Cases of IE in children and adults with CHD were prospectively recorded as part of the UK National Institute for Cardiovascular Outcomes Research (NICOR) National Congenital Heart Disease Audit. Patients were entered into the database between April 2008 and March 2016.

**RESULTS:** Eight hundred episodes of IE were recorded in 736 patients with CHD. Sixty-five patients (9%) were infants (aged <1 year), 235 (32%) were children (aged 1-15 years), and 436 (59%) were adults (aged >15 years). The most common diagnoses were Tetralogy of Fallot (n = 150, 22.8%), ventricular septal defect (n = 129, 19.6%) and bicuspid aortic valve (n = 70, 10.7%). Dental procedures preceded 67 of 635 episodes (11%) of IE, and non-dental invasive procedures preceded 177 of 644 episodes (27.4%). The most common causative organisms were streptococci, accounting for 40% of cases. Overall in-hospital mortality was 6.7%. On multivariable analysis, adverse factors associated with in-hospital mortality were staphylococcal infection and presence of an underlying atrioventricular septal defect.

**CONCLUSIONS:** Infective endocarditis in patients with CHD is an ongoing clinical challenge. In contemporary practice in tertiary congenital centers, 1 of 15 patients do not survive to hospital discharge. Streptococci remain the most common causative organism, and antecedent dental or medical procedures were undertaken in a significant minority in the 3 months before diagnosis. The presence of an atrioventricular septal defect or staphylococcal infection is associated with significantly increased risk of early mortality.

PMID: 31299559

## **Dietary Vitamin B6 Intake Associated with a Decreased Risk of Cardiovascular Disease: A Prospective Cohort Study.**

Jeon J, Park K.

Although the biological mechanisms underlying the beneficial effects of vitamin B6 on cardiovascular disease (CVD) have been reported on, epidemiological studies have yielded controversial results, and data on the Korean population are limited. This study examined the association between dietary vitamin B6 intake and CVD incidence in Koreans. A total of 9142 participants of the Korean Genome and Epidemiology Study, aged 40-69 years, who did not have CVD or cancer at the baseline were included in the analysis. Dietary data were assessed using a validated semi-quantitative food frequency questionnaire. CVD incidence was assessed using biennial questionnaires and confirmed through repeated personal interviews. Multivariable-adjusted hazard ratios (HRs) and 95% confidence intervals (CIs) were estimated using Cox proportional hazard regression models. After multivariate adjustment, a higher vitamin B6 intake was significantly associated with a decreased CVD risk in men (HR: 0.44; 95% CI: 0.25-0.78); no such association was observed in women. Dose-response analysis confirmed the presence of inverse linearity between vitamin B6 intake and CVD incidence in men ( $p$  for nonlinearity = 0.3). A higher dietary intake level of vitamin B6 was associated with a reduced CVD risk in Korean men. These observations require further verification in other populations.

PMID: 31261898

## **Prevalence of Cardiovascular Risk Factors Among Cancer Patients in the United States.**

Rubens M, Appunni S, Ramamoorthy V, Saxena A, Das S, Bhatt C, Boulanger BK, Viamonte-Ros A, Veledar E.

**Background:** Cancer and cardiovascular diseases (CVDs) are leading causes of morbidity and mortality. We analyzed national data to examine the prevalence of CVD risk factors among adult cancer survivors in the United States.

**Methods:** Participants included adults  $\geq 18$  years of age from the National Health and Nutrition Examination Survey 2001-2002 to 2013-2014. CVD risk factors included hypertension, diabetes, dyslipidemia, obesity, smoking, and physical activity. Prevalence of 1, 2, or  $\geq 3$  CVD risk factors was compared between cancer and noncancer participants. All CVD risk factors were adjusted for age and smoking and additionally for sex. Differences in CVD risk factors among cancer and noncancer participants were identified using logistic regression analysis.

**Results:** Among 35,379 eligible participants, 2906 (8.4%) had a history of cancer. The proportion of participants having a single CVD risk factor was lower among cancer survivors compared with noncancer participants (25.8% vs. 33.9%,  $P < 0.001$ ). The proportions of participants having two CVD risk factors (33.5% vs. 24.6%,  $P < 0.001$ ) and  $\geq 3$  CVD risk factors (27.4% vs. 16.4%,  $P < 0.001$ ) were higher among cancer survivors. However, these associations lost significance upon adjusting for age. The odds of total hypertension (odds ratio [OR] 1.25, 95% confidence interval [CI]: 1.11-1.40) and total diabetes (OR 1.33, 95% CI: 1.08-1.65) were significantly higher among cancer survivors.

**Conclusions:** Our study showed that adult cancer survivors in the United States had higher levels of CVD risk factors primarily due to age-related factors, in addition to cancer complications. There is a significant need for improved CVD risk assessment and prevention services for cancer survivors.

PMID: 31241405



## **A Vascular Aging Index as Independent Predictor of Cardiovascular Events and Total Mortality in an Elderly Urban Population.**

Nilsson Wadström B, Fatehali AH, Engström G, Nilsson PM.

The morphology and function of the arteries can be directly measured using different established methods. This prospective cohort study aimed to translate 2 of these, aortic pulse wave velocity (aPWV) and carotid intima-media thickness (cIMT), into a combined Vascular Aging Index (VAI) and then evaluate the predictive power of aPWV, cIMT, and VAI. Patients (n = 2718) were included from the cardiovascular arm of the Malmö Diet and Cancer Study (median age 71.9 years, 62.2% females). Total follow-up time was 16 448 person-years and a composite cardiovascular disease (CVD) end point was used. Cox regressions yielded adjusted hazard ratios (95% confidence interval) per 1 standard deviation increment of loge aPWV, loge cIMT, and loge VAI of 1.25 (1.08-1.45, P = .003), 1.27 (1.13-1.44, P < .001), and 1.45 (1.26-1.68, P < .001), respectively. The C-statistics increased from 0.714 to 0.734 when adding aPWV and cIMT to a model of conventional risk factors. Net Reclassification Index also showed a significant (P < .001) improvement for the classification of event-free patients and no change for patients with events. A VAI based on aPWV and cIMT had a good predictive performance. Used together, aPWV and cIMT incrementally and significantly improve the prediction of CVD events by correctly down-adjusting the predicted risk for noncases.

PMID: 31234636

## **Risk of cardiovascular disease outcomes in primary care subjects with familial hypercholesterolaemia: A cohort study.**

Iyen B, Qureshi N, Kai J, Akyea RK, Leonardi-Bee J, Roderick P, Humphries SE, Weng S.

**BACKGROUND AND AIMS:** Familial hypercholesterolaemia (FH) is a known major cause of premature heart disease. However, the risks of atherosclerotic disease in other vascular regions are less known. We determined the risk of major cardiovascular disease (CVD) outcomes associated with clinical FH.

**METHODS:** In a retrospective cohort study (1 January, 1999 to 22 July, 2016), we randomly-matched 14,097 UK subjects with clinical FH diagnoses or characteristics (Simon-Broome definite or Dutch Lipid Clinic Score >8) to 42,506 subjects without FH by age, sex, general practice. We excluded those with CVD at baseline. Incident rates for coronary heart disease (CHD), stroke or transient ischaemic attack (TIA) and peripheral vascular disease (PVD) were estimated. Cox proportional hazards regression, stratified on matched-pairs, determined adjusted hazards ratios (HR) for incident CVD.

**RESULTS:** During follow-up (median 13.8 years), incidence rates (95% CI) of CVD (per 1000 person-years) were 25.6 (24.8-26.3) in FH and 2.9 (2.8-3.1) in non-FH subjects. The risk of CHD, stroke/TIA and PVD was higher in FH compared to non-FH subjects: CHD (HR 10.63, 95% CI 9.82-11.49), stroke/TIA (HR 6.74, 95% CI 5.84-7.77), PVD (HR 7.17, 95% CI 6.08-8.46). The risk of CVD was greater in those with FH characteristics (HR 13.52, 95% CI 12.48-14.65) than those with clinical diagnoses (HR 1.66, 95% CI 1.42-1.93).

**CONCLUSIONS:** In addition to the recognised increased risk of CHD, subjects with FH have greatly elevated risk of stroke/TIA and PVD. This emphasises need for early diagnosis and preventive interventions beyond CHD, to reduce CVD risk in these individuals.

PMID: 31181417

## **Racial and ethnic differences in cardiovascular disease and outcome in type 1 diabetes patients.**

Ali MT, Al Suwaidi J.

**INTRODUCTION:** Type 1 diabetes mellitus (T1DM) has increased dramatically over the last two decades with global variation greater than 350-fold difference reflecting the ethnic, racial, and geographical variation. Diabetic patients remain at a higher risk of cardiovascular mortality than those without diabetes. Therefore, it is vital for clinicians to have in-depth knowledge of T1DM statistics and their impact on people health and health resources.

**AREAS COVERED:** This review will cover the epidemiologic characteristics of T1DM and the influence of race, ethnicity, and geographical variation on the incidence and the outcome. The minority populations health disparities in the clinical presentation and outcomes among youth with T1DM, the long-term glycemic control patterns in racially and ethnically diverse youth, and the long-term influence of these factors on cardiovascular outcomes will be elucidated. The PubMed database was searched using the terms: T1DM ± incidence, Race, ethnicity, and Genetic.

**EXPERT OPINION:** Understanding the epidemiological characteristics of T1DM including race, ethnicity and the genetic predisposition will help to develop guidelines target these higher risk patients of an unfavorable outcome. Further research and interventional strategies to identify infants at genetic risk of T1DM may help to prevent, stop or retard the destructive autoimmune process leading to T1DM.

PMID: 31081398

## **Is depression a real risk factor for acute myocardial infarction mortality? A retrospective cohort study.**

Cocchio S, Baldovin T, Furlan P, Buja A, Casale P, Fonzo M, Baldo V, Bertoncetto C.

**BACKGROUND:** Depression has been associated with a higher risk of cardiovascular events and a higher mortality in patients with one or more comorbidities. This study investigated whether continuative use of antidepressants (ADs), considered as a proxy of a state of depression, prior to acute myocardial infarction (AMI) is associated with a higher mortality afterwards. The outcome to assess was mortality by AD use.

**METHODS:** A retrospective cohort study was conducted in the Veneto Region on hospital discharge records with a primary diagnosis of AMI in 2002-2015. Subsequent deaths were ascertained from mortality records. Drug purchases were used to identify AD users. A descriptive analysis was conducted on patients' demographics and clinical data. Survival after discharge was assessed with a Kaplan-Meier survival analysis and Cox's multiple regression model.

**RESULTS:** Among 3985 hospital discharge records considered, 349 (8.8%) patients were classified as 'AD users'. The mean AMI-related hospitalization rate was 164.8/100,000 population/year, and declined significantly from 204.9 in 2002 to 130.0 in 2015, but only for AD users (-40.4%). The mean overall follow-up was  $4.6 \pm 4.1$  years. Overall, 523 patients (13.1%) died within 30 days of their AMI. The remainder survived a mean  $5.3 \pm 4.0$  years. After adjusting for potential confounders, use of antidepressants was independently associated with mortality (adj OR=1.75, 95% CI: 1.40-2.19).

**CONCLUSIONS:** Our findings show that AD users hospitalized for AMI have a worse prognosis in terms of mortality. The use of routinely-available records can prove an efficient way to monitor trends in the state of health of specific subpopulations, enabling the early identification of AMI survivors with a history of antidepressant use.

PMID: 31014311

## **Low-Carbohydrate Diets and Risk of Incident Atrial Fibrillation: A Prospective Cohort Study.**

Zhang S, Zhuang X, Lin X, Zhong X, Zhou H, Sun X, Xiong Z, Huang Y, Fan Y, Guo Y, Du Z, Liao X.

**Background** The influences of low-carbohydrate diets in cardiovascular disease are controversial. Few studies have examined the relationship of carbohydrate intake and risk of incident atrial fibrillation (AF). We aimed to evaluate the association between carbohydrate intake and the risk of incident AF in the ARIC (Atherosclerosis Risk in Communities) Study. **Methods and Results:** We included 13 385 participants (age, 54.2±5.8 years; 45.1% men and 74.7% white) who completed a dietary questionnaire at baseline (1987-1989) in the ARIC Study. The primary outcome was incident AF, which was identified by ECG performed during study examinations, hospital discharge codes, and death certificates. We used multivariable Cox hazard regression models to assess the association between carbohydrate intake and incident AF. We further explored the effects of specific food source (animal versus plant based) used to replace carbohydrate intake in the low-carbohydrate intake setting. During a median follow-up of 22.4 years, 1808 cases (13.5%) of AF occurred. The hazard ratio for incident AF associated with a 1- SD (9.4%) increase in carbohydrate intake as a percentage of energy intake was 0.82 (95% CI, 0.72-0.94), after adjustment for traditional AF risk factors and other diets factors.

Results were similar when individuals were categorized by carbohydrate intake quartiles (hazard ratio, 0.64; 95% CI, 0.49-0.84; comparing extreme quartiles). No association was found between the type of protein or fat used to replace the carbohydrate and risk of incident AF.

**Conclusions** Low-carbohydrate diets were associated with increased risk of incident AF, regardless of the type of protein or fat used to replace the carbohydrate.

PMID: 31020911

## **Association of Low Fasting Glucose and HbA1c With Cardiovascular Disease and Mortality: The MESA Study.**

Mongraw-Chaffin M, Bertoni AG, Golden SH, Mathioudakis N, Sears DD, Szklo M, Anderson CAM.

Trials of intensive glucose control have not improved cardiovascular disease (CVD) risk in populations with type 2 diabetes; however, in the general population, reports are inconsistent about the effects of maintaining lower glucose levels. Some speculate that low glycemic values are associated with increased glycemic variability, which is in turn associated with higher CVD risk. It has also been suggested that fasting glucose and hemoglobin A1c (HbA1c) in the lower ranges have a different relationship with CVD and mortality. In 4990 participants from the Multi-Ethnic Study of Atherosclerosis, we used logistic regression to investigate associations of low fasting glucose (<80 mg/dL) and HbA1c (<5.0%) from baseline and averaged across follow-up with incident CVD and mortality over 13 years. We used normal glycemic ranges (80 to <100 mg/dL and 5.0 to <5.7%) as references and analyzed glycemic levels with visit-matched covariates. We adjusted for potential confounding by age, sex, race/ethnicity, education, income, smoking status, body mass index, total cholesterol level, cholesterol medications, high-density lipoprotein cholesterol, and hypertension. Low baseline glucose and HbA1c were positively, but not significantly, associated with mortality, whereas low average fasting glucose and HbA1c were strongly and significantly associated with incident CVD [glucose OR, 2.04 (95% CI, 1.38-3.00); HbA1c OR, 2.01 (95% CI, 1.58-2.55)] and mortality [glucose OR, 1.93 (95% CI, 1.33-2.79); HbA1c OR, 2.51 (95% CI, 2.00-3.15)]. These results were not due to type 2 diabetes or medication use. Glucose variability did not explain CVD risk beyond average glucose levels. Chronic low fasting glucose and HbA1c may be better indicators of risk than a single low measurement.

PMID: 31020054

## **Association between prediabetes (defined by HbA1C, fasting plasma glucose, and impaired glucose tolerance) and the development of chronic kidney disease: a 9-year prospective cohort study.**

Kim GS, Oh HH, Kim SH, Kim BO, Byun YS.

**BACKGROUND:** The aim of the present study was to investigate the clinical impact of prediabetes on the development of incident chronic kidney disease (CKD) in a Korean adult population, using data from the Korea Genome and Epidemiology Study.

**METHODS:** This prospective cohort study included 7728 Korean adults without baseline CKD and type 2 diabetes. Prediabetes was defined by impaired fasting glucose (IFG), impaired glucose tolerance (IGT), and HbA1C level. CKD was defined as estimated glomerular filtration rate <60 mL/min/1.73 m<sup>2</sup>. We assessed the predictive value of prediabetes for the incidence of CKD, and investigated the incidence of cardiovascular disease including coronary artery disease and stroke.

**RESULTS:** Over a median follow-up period of 8.7 years, 871 of 7728 (11.3%) subjects developed incident CKD. Patients with prediabetes, as defined by IGT or HbA1C, developed incident CKD more frequently than the non-prediabetic group did. The risk of CKD development at follow-up was analyzed according to different prediabetes definitions. Compared with the non-prediabetic group, the IGT- (Hazard ratio [HR]=1.135, 95% confidence interval [CI]=1.182-1.310, P=0.043) and HbA1C-defined prediabetic groups (HR=1.391, 95% CI=1.213-1.595, P<0.001) were significantly associated with incident CKD after adjusting for traditional CKD risk factors; however, IFG was not associated with incident CKD.

**CONCLUSION:** IGT- or HbA1C-defined prediabetes is an independent predictor of incident CKD. The measurement of these parameters might enable early detection of CKD risk, allowing physicians to initiate preventive measures and improve patient outcomes.

PMID: 30992067

## **Population susceptibility differences and effects of air pollution on cardiovascular mortality: epidemiological evidence from a time-series study.**

Liu M, Xue X, Zhou B, Zhang Y, Sun B, Chen J, Li X.

There is insufficient evidence on the relationship between air pollution and mortality from cardiovascular disease (CVD) in northeast China. Here, we explored the short-term effects of air pollution on CVD mortality and preliminarily investigated differences in population susceptibility to air pollution in Shenyang, China. CVD mortality, air pollution, and meteorological data during 2013-2016 were obtained. Time-series analysis was applied to evaluate the association between air pollution and daily CVD mortality with different lag structures. In the single-pollutant model, each 10  $\mu\text{g}/\text{m}^3$  increase in PM<sub>2.5</sub>, PM<sub>10</sub>, SO<sub>2</sub>, NO<sub>2</sub>, and O<sub>3</sub> concentrations and 1 mg/m<sup>3</sup> increase in CO concentrations at lag<sub>0</sub> (same day) was significantly associated with an increase of 0.40% (95% confidence interval, 0.22-0.59%), 0.26% (0.12-0.40%), 0.43% (0.16-0.70%), 0.90% (0.14-1.67%), 0.76% (0.21-1.32%), and 3.33% (0.97-5.75%), respectively, in overall CVD mortality. Susceptibility to air pollutants was higher among females, elderly people, and ischemic heart disease patients. Furthermore, air pollution effects on CVD mortality were 2-8 times greater during the non-heating period. In conclusion, the air pollutants PM<sub>2.5</sub>, PM<sub>10</sub>, SO<sub>2</sub>, NO<sub>2</sub>, O<sub>3</sub>, and CO showed significant positive effects on CVD mortality in Shenyang, China. These findings highlight the adverse effects of air pollution and suggest the need for personal protective equipment and reduction of air pollution sources.

PMID: 30963427 [Indexed for MEDLINE]



## **Cardiovascular health and sleep disturbances in two population-based cohort studies.**

Hausler N, Lisan Q, Van Sloten T, Haba-Rubio J, Perier MC, Thomas F, Danchin N, Guibout C, Boutouyrie P, Heinzer R, Jouven X, Marques-Vidal P, Empana JP.

**OBJECTIVE:** We aimed to investigate the association between cardiovascular health (CVH), as defined by the American Heart Association, and several sleep disturbances.

**METHODS:** Two community-based cohorts, the Paris Prospective Study 3 (PPS3, France, n=6441) and the CoLaus study (Switzerland, n=2989) were analysed. CVH includes 7 metrics which all can be classified as poor, intermediate and ideal. Global CVH score was categorised into poor (0-2 ideal metrics), intermediate (3-4 ideal metrics) and ideal ( $\geq 5$  ideal metrics). Associations between global CVH and self-reported sleep disturbances (proxy of sleep-disordered breathing [SDB], excessive daytime sleepiness, insomnia symptoms and short/long sleep duration) and SDB severity measured by polysomnography (PSG) were investigated. Adjusted OR/relative risk ratio (RRR) and 95% CIs were estimated. Subjects with previous cardiovascular disease were excluded.

**RESULTS:** Compared with poor CVH, subjects with intermediate and ideal global CVH had lower odds of self-reported SDB in both cohorts (ORs 0.55; 95%CI 0.44 to 0.68 and 0.35; 95%CI 0.22 to 0.53, respectively) and had lower SDB severity measured by PSG (RRR 0.07; 95%CI 0.02 to 0.20) in CoLaus. Subjects with intermediate and ideal global CVH had lower odds of excessive daytime sleepiness in PPS3 (ORs 0.82; 0.72 to 0.95 and 0.80; 0.82 to 1.02, respectively). No consistent associations were found between CVH and sleep duration or insomnia symptoms.

**CONCLUSIONS:** Higher levels of CVH are associated with lower odds of SDB and excessive daytime sleepiness. However, causal interpretation cannot be made and associations might be bidirectional.

PMID: 30962189



## *Outcomes Cardiovasculares*

Pesquisa Bibliográfica efectuada em Pubmed ([www.ncbi.nlm.nih.gov/](http://www.ncbi.nlm.nih.gov/)) -Abr a Jun 2019

## **Relation of Vegetarian Dietary Patterns With Major Cardiovascular Outcomes: A Systematic Review and Meta-Analysis of Prospective Cohort Studies.**

Glenn AJ, Vigiouliouk E, Seider M, Boucher BA, Khan TA, Blanco Mejia S, Jenkins DJA, Kahleová H, Rahelić D, Salas-Salvadó J, Kendall CWC, Sievenpiper JL.

**Background:** Vegetarian dietary patterns are recommended for cardiovascular disease (CVD) prevention and management due to their favorable effects on cardiometabolic risk factors, however, the role of vegetarian dietary patterns in CVD incidence and mortality remains unclear. **Objective:** To update the European Association for the Study of Diabetes (EASD) clinical practice guidelines for nutrition therapy, we undertook a systematic review and meta-analysis of the association of vegetarian dietary patterns with major cardiovascular outcomes in prospective cohort studies that included individuals with and without diabetes using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) approach. **Methods:** MEDLINE, EMBASE, and Cochrane databases were searched through September 6th, 2018. We included prospective cohort studies  $\geq 1$  year of follow-up including individuals with or without diabetes reporting the relation of vegetarian and non-vegetarian dietary patterns with at least one cardiovascular outcome. Two independent reviewers extracted data and assessed study quality (Newcastle-Ottawa Scale). The pre-specified outcomes included CVD incidence and mortality (total CVD, coronary heart disease (CHD) and stroke). Risk ratios for associations were pooled using inverse variance random effects model and expressed as risk ratios (RRs) with 95% confidence intervals (CIs). Heterogeneity was assessed (Cochran Q-statistic) and quantified (I<sup>2</sup>-statistic). The overall certainty of the evidence was assessed using GRADE. **Results:** Seven prospective cohort studies (197,737 participants, 8,430 events) were included. A vegetarian dietary pattern was associated with reduced CHD mortality [RR, 0.78 (CI, 0.69, 0.88)] and incidence [0.72 (0.61, 0.85)] but were not associated with CVD mortality [0.92 (0.84, 1.02)] and stroke mortality [0.92 (0.77, 1.10)]. The overall certainty of the evidence was graded as "very low" for all outcomes, owing to downgrades for indirectness and imprecision. **Conclusions:** Very low-quality evidence indicates that vegetarian dietary patterns are associated with reductions in CHD mortality and incidence but not with CVD and stroke mortality in individuals with and without diabetes. More research, particularly in different populations, is needed to improve the certainty in our estimates. Clinical Trial Registration: Clinicaltrials.gov, identifier: NCT03610828.

PMCID: PMC6585466

PMID: 31263700

## **Upstroke time per cardiac cycle is associated with cardiovascular prognosis in type 2 diabetes.**

Chang LH, Hwu CM, Chu CH, Won JGS, Chen HS, Lin LY.

Objective Upstroke time per cardiac cycle (UTCC) in the lower extremities has been found to be predictive of cardiovascular mortality in the general population. Therefore, the purpose of the study was to test the associations between increasing UTCC and outcomes in patients with type 2 diabetes. Design and methods A total of 452 patients with type 2 diabetes (age:  $67.5 \pm 8.6$  years; male: 54%) registered in share-care program participated in the study at an out-patient clinic in Taipei Veterans General Hospital across a mean of 5.8 years. Primary outcomes were all-cause mortality hospitalization for coronary artery disease, stroke, revascularization, amputation and diabetic foot syndrome. Secondary end-point outcome was all-cause mortality. Results Increment of UTCC associations with primary and secondary outcome were undertaken prior to baseline characteristic adjustments. A UTCC of 20.1% exhibited the greatest area under curve (AUC), sensitivity, and specificity balance to predict composite events in receiver operating curves (AUC: 0.63,  $p=0.001$ ; sensitivity: 67.7%; specificity: 54.9%). Sixty-four composite events and 17 deaths were identified from medical records.  $UTCC \geq 20.1\%$  was associated with the occurrence of composite events and an increased risk of mortality. For composite events, an adjusted hazard ratio (HR) of 2.45 and 95% confidence interval (CI) of 1.38-4.35 ( $p=0.002$ ) were calculated. For all-cause mortality, an adjusted HR of 1.91 and 95% CI of 0.33-10.99 ( $p=0.467$ ) were calculated. Conclusions Increasing UTCC was associated with cardiovascular outcomes in patients with type 2 diabetes. Therefore, UTCC is advocated as a noninvasive screening tool for ambulatory patients with type 2 diabetes.

PMID: 31241364

## **Impact of Lunar Phase on Outcomes Following ST-Elevation Myocardial Infarction.**

Segan L, Brennan A, Reid CM, Hiew C, Oqueli E, Ajani A, Clark D, Duffy SJ, Yip T.

**BACKGROUND:** There is a long-held belief in the association between the full moon and extremes of human behaviour and adverse health consequences. Small-scale studies are conflicting, however most suggest no clear association between lunar phase and occurrence of acute coronary syndromes.

**METHODS:** We conducted a multi-centre retrospective study from the Melbourne Intervention Group registry, including 7,570 ST-elevation myocardial infarction (STEMI) cases from 6 tertiary centres over a 12-year study period in Victoria, Australia and performed statistical analysis using Stata software.

**MAIN OUTCOME MEASURES:** Primary outcomes studied were the incidence of STEMI, the occurrence of major adverse cardiac and cerebrovascular events and mortality at 1 and 5 years in cases of ST-elevation myocardial infarction undergoing primary or rescue percutaneous coronary intervention during the full moon between 2005-2017 in Victoria, Australia.

**RESULTS:** This study demonstrated no significant difference in STEMI incidence ( $p=0.61$ ) nor of major adverse cardiovascular events across all lunar phases. Subgroup analysis confirmed no difference in outcomes during the full moon compared to a composite of other lunar phases. Kaplan-Meier survival estimates showed similar 30-day outcomes across lunar phases ( $p=0.35$ ) and when comparing full moon to a composite of other lunar phases ( $p=0.45$ ). Similarly, there was no significant difference in survival at 1 and 5 years between lunar phases ( $p=0.68$ ) or compared to the full moon phase ( $p=0.51$ ).

**CONCLUSIONS:** This study showed no significant difference in the incidence or cardiovascular outcomes and survival in patients with ST-elevation myocardial infarction undergoing primary or rescue percutaneous coronary intervention during the lunar phases. This article is protected by copyright. All rights reserved.

PMID: 31237407

## **Vitamin D Supplementation and Cardiovascular Disease Risks in More Than 83 000 Individuals in 21 Randomized Clinical Trials: A Meta-analysis.**

Barbarawi M, Kheiri B, Zayed Y, Barbarawi O, Dhillon H, Swaid B, Yelangi A, Sundus S, Bachuwa G, Alkotob ML, Manson JE.

**Importance:** Observational studies have reported an association between low serum vitamin D levels and elevated risk of cardiovascular disease (CVD) events, but such studies cannot prove causation because of possible unmeasured confounding.

**Objective:** We conducted a meta-analysis of randomized clinical trials that tested the association of vitamin D supplementation with reduced CVD events and all-cause mortality.

**Data Sources:** Literature search through PubMed, the Cochrane Library, and Embase was completed by 2 reviewers from each database's inception to December 15, 2018.

**Study Selection:** Inclusion criteria were randomized clinical trials that reported the effect of long-term ( $\geq 1$  year) vitamin D supplementation on CVD events and all-cause mortality. Studies that did not include cardiovascular outcomes were excluded.

**Data Extraction and Synthesis:** Data were abstracted independently by 2 authors. Random-effects models were used to report the risk ratios (RRs) and 95% CIs. Main Outcomes and Measures:

Major adverse cardiovascular events was the primary outcome, and rates of myocardial infarction, stroke or cerebrovascular accident, CVD mortality, and all-cause mortality were the secondary end points. **Results:** Twenty-one randomized clinical trials were included (including 83 291 patients, of whom 41 669 received vitamin D and 41 622 received placebos). The mean (SD) age of trial participants was 65.8 (8.4) years; 61 943 (74.4%) were female. Only 4 trials had prespecified CVD as a primary end point. Vitamin D supplementation compared with placebo was not associated with reduced major adverse cardiovascular events (RR, 1.00 [95% CI, 0.95-1.06];  $P = .85$ ) nor the secondary end points of myocardial infarction (RR, 1.00 [95% CI, 0.93-1.08];  $P = .92$ ), stroke (RR, 1.06 [95% CI, 0.98-1.15];  $P = .16$ ), CVD mortality (RR, 0.98 [95% CI, 0.90-1.07];  $P = .68$ ), or all-cause mortality (RR, 0.97 [95% CI, 0.93-1.02];  $P = .23$ ). Results were generally consistent by sex, baseline 25-hydroxyvitamin D level, vitamin D dosage, formulation (daily vs bolus dosing), and presence or absence of concurrent calcium administration.

**Conclusions and Relevance:** In this updated meta-analysis, vitamin D supplementation was not associated with reduced major adverse cardiovascular events, individual CVD end points (myocardial infarction, stroke, CVD mortality), or all-cause mortality. The findings suggest that vitamin D supplementation does not confer cardiovascular protection and is not indicated for this purpose. PMID: 31215980

## **A whole-food, plant-based nutrition program: Evaluation of cardiovascular outcomes and exploration of food choices determinants.**

Morin É, Michaud-Létourneau I, Couturier Y, Roy M.

**OBJECTIVES:** An ideal diet to prevent cardiovascular diseases contains an unlimited intake of various plant foods and a reduced intake of animal and highly processed foods. Researchers have reported that nutrition education programs that prioritize whole-plant foods effectively contribute to the prevention of unhealthy cardiovascular outcomes. We examined whether a 12-wk nutrition education program in adults from Montreal (Quebec, Canada) with at least one risk factor of cardiovascular disease was effective in modifying their eating patterns toward including more whole-plant foods. We further evaluated the effects of this program on participants' cardiovascular outcomes and explored determinants influencing food choices toward whole-food, plant-based diets.

**METHODS:** A sequential, explanatory, mixed-methods, research design was used. A quantitative step (i.e., single-arm, quasi-experimental trial) preceded participant recruitment for a qualitative phase (i.e., phenomenological study; semistructured interview; thematic analysis). The examined outcomes were changes in cardiovascular risk factors (paired t tests) and determinants of food choice (thematic analysis).

**RESULTS:** Weight (-10.5 lbs; 95% confidence interval [CI]: -9.0 to -12.0), waist circumference (-7.4 cm; 95% CI: -6.5 to -8.4), total cholesterol (-0.87 mmol/L; 95% CI: -0.57 to -1.17), and low-density lipoprotein cholesterol (-29.7% or -0.84 mmol/L; 95% CI: -0.55 to -1.13) all improved significantly ( $P < 0.001$ ). Encouraging ad libitum intake of various whole-food plant-based items appealed more to participants than traditional strategies. Altruistic and societal motives, in addition to health, were identified as key determinants of an increased adoption of whole-food plant-based diets.

**CONCLUSIONS:** The whole-food, plant-based nutrition program improves cardiovascular health in adults and features characteristics that may inform future nutrition programs and public health interventions.

PMID: 31207440

## **Associations of Gout and Baseline Serum Urate Level With Cardiovascular Outcomes: Analysis of the Coronary Disease Cohort Study.**

Stamp LK, Frampton C, Drake J, Doughty RN, Troughton RW, Richards AM.

**OBJECTIVE:** To determine whether gout and serum urate (SU) levels are associated with increased risk of death, time to first readmission for any cardiovascular event, or incident heart failure in individuals with cardiovascular disease.

**METHODS:** Individuals presenting with an acute coronary syndrome (ACS) were enrolled in the Coronary Disease Cohort Study. Clinical data were collected from the medical records at the index hospital admission, and clinical, echocardiographic, and biochemical data were collected postdischarge. Gout was defined by self-report, use of urate-lowering therapy, or use of colchicine with evidence of gout on review of the medical record. The primary end points were all-cause mortality, time to readmission for a cardiac ischemic event, and time to readmission for heart failure.

**RESULTS:** Data from 1,514 participants were available. During the follow-up period, 53 of 160 participants with gout (33.1%) and 298 of 1,354 participants without gout (22.0%) died. After adjustment for other factors known to be associated with mortality, there was no gout-specific increase in risk of mortality (adjusted hazard ratio 0.98 [95% confidence interval 0.69-1.38]). Time to readmission for heart failure was significantly briefer in those with, compared to those without, gout (adjusted hazard ratio 1.42 [95% confidence interval 1.02-1.97]). Irrespective of whether a participant had gout or not, as SU level increased, there was an increased risk of death and readmission for either a cardiovascular event or heart failure.

**CONCLUSION:** Survival post-ACS is similar with and without the presence of gout. People with gout are at an increased risk of readmission for heart failure and have longer hospital stays. Risk of these events increases in parallel with increases in SU levels.

PMID: 31162825



## **Aspirin has potential benefits for primary prevention of cardiovascular outcomes in diabetes: updated literature-based and individual participant data meta-analyses of randomized controlled trials.**

Seidu S, Kunutsor SK, Sesso HD, Gaziano JM, Buring JE, Roncaglioni MC, Khunti K.

**BACKGROUND:** The clinical benefit of aspirin for the primary prevention of cardiovascular disease (CVD) in diabetes remains uncertain. To evaluate the efficacy and safety of aspirin for the primary prevention of cardiovascular outcomes and all-cause mortality events in people with diabetes, we conducted an updated meta-analysis of published randomised controlled trials (RCTs) and a pooled analysis of individual participant data (IPD) from three trials.

**METHODS:** Randomised controlled trials of aspirin compared with placebo (or no treatment) in participants with diabetes with no known CVD were identified from MEDLINE, Embase, Cochrane Library, and manual search of bibliographies to January 2019. Relative risks with 95% confidence intervals were used as the summary measures of associations.

**RESULTS:** We included 12 RCTs based on 34,227 participants with a median treatment duration of 5.0 years. Comparing aspirin use with no aspirin, there was a significant reduction in risk of major adverse cardiovascular events (MACE) 0.89 (0.83-0.95), with a number needed to treat (NNT) of 95 (95% CI 61 to 208) to prevent one MACE over 5 years average follow-up. Evidence was lacking of heterogeneity and publication bias among contributing trials for MACE. Aspirin use had no effect on other endpoints including all-cause mortality; however, there was a significant reduction in stroke for aspirin dosage  $\leq 100$  mg/day 0.75 (0.59-0.95). There were no significant effects of aspirin use on major bleeding and other bleeding events, though some of the estimates were imprecise. Pooled IPD from the three trials (2306 participants) showed no significant evidence of an effect of aspirin on any of the outcomes evaluated; however, aspirin reduced the risk of MACE in non-smokers 0.70 (0.51-0.96) with a NNT of 33 (95% CI 20 to 246) to prevent one MACE.

**CONCLUSIONS:** Aspirin has potential benefits in cardiovascular primary prevention in diabetes. The use of low dose aspirin may need to be individualised and based on each individual's baseline CVD and bleeding risk. Systematic review registration PROSPERO: CRD42019122326.

PMID: 31159806

## **Assessment of Heart Failure in Diabetes Cardiovascular Outcomes Trials: Is What We Are Currently Capturing Adequate?**

Bowes CD, Lien LF, Butler J.

**PURPOSE OF REVIEW:** Since the 2008 FDA guidance restructuring the design of trials for the approval of novel glucose-lowering agents, 13 medications have now been evaluated by dedicated cardiovascular outcome trials. All of the completed trials have included data (though with varying definitions) on rates of hospitalization for heart failure. This review is aimed at summarizing current heart failure outcome data available from cardiovascular safety trials for novel glucose-lowering agents in patients with type 2 diabetes mellitus.

**RECENT FINDINGS:** There appears to be growing evidence for the benefit of sodium-glucose cotransporter-2 inhibitors, and there are still not enough data to fully support the safety of glucagon-like peptide 1 receptor agonists in heart failure. Increased rates of hospitalization for heart failure were seen with both saxagliptin and alogliptin, and this has led to a class warning for all dipeptidyl peptidase-4 inhibitors. Future studies should have a standardized definition of "hospitalization for heart failure," should consider including hospitalization for heart failure as a component of the primary composite endpoint, and should provide a more detailed description of the baseline characteristics of enrolled study participants with heart failure.

PMID: 31127397

## **Risk assessment of energy drinks with focus on cardiovascular parameters and energy drink consumption in Europe.**

Ehlers A, Marakis G, Lampen A, Hirsch-Ernst KI.

To assess the possible cardiovascular risks associated with energy drink (ED) consumption in Europe, a comprehensive literature research was performed in regard to (i) possible ED-induced dose-dependent cardiovascular outcomes, (ii) ED consumption patterns in Europe and (iii) the risks of EDs in combination with alcohol. The identified intervention studies primarily investigated acute ED effects in young healthy adults. Moderate consumption of EDs corresponding to an acute caffeine intake of up to 200 mg did not result in clinically relevant cardiovascular changes in young healthy adults. However, high intake of EDs (about 1 L) was associated with moderate to severe adverse effects in some participants (i.a. prolonged QTc interval, palpitations). Studies have indicated that on some occasions, a substantial proportion of ED consuming children and adolescents (12% in 16 EU Member States) drink EDs in high quantities ( $\geq 1$  L). This could pose a possible health risk to this group since adverse effects by such high ED consumption have been observed already in young healthy adults. Among further measures that might be considered to minimize this identified risk, policy makers could develop information and educational programs with the aim of raising public awareness.

PMID: 31112702 [Indexed for MEDLINE]

## **Low-density lipoprotein cholesterol lowering for the prevention of cardiovascular outcomes in patients with ischemic stroke.**

Ntaios G, Milionis H.

**BACKGROUND:** Low-density lipoprotein (LDL) cholesterol has been long associated with the risk for ischemic stroke, myocardial infarction, and cardiovascular death. For more than a decade, the main pharmacological option to prevent stroke and myocardial infarction through LDL-cholesterol lowering was the use of statins. During the recent years, two novel classes of drugs have proven their efficacy and safety to reduce LDL-cholesterol and prevent cardiovascular events in large, well-conducted randomized controlled trials: ezetimibe and proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors.

**AIMS:** The present review summarizes the evidence arising from the latest trials of lipid-lowering treatment for cardiovascular outcomes prevention and discusses their implications for secondary prevention strategies in patients with ischemic stroke.

**SUMMARY OF REVIEW:** There is strong evidence which confirms the hypothesis that the lower the LDL-cholesterol, the less frequent the cardiovascular events are and underlines the importance of treating our ischemic stroke patients with intensive statin treatment aiming at low LDL-cholesterol levels. The very low levels of LDL cholesterol seem to be safe, even in the mid/long term but longer follow-up data are needed. Currently there are no tools to reliably predict cardiovascular outcomes in the specific population of ischemic stroke patients.

**CONCLUSIONS:** Stroke physicians should aim for low LDL-cholesterol levels by intensive statin treatment in all ischemic stroke patients. For those patients who are at the highest risk for recurrent stroke or another cardiovascular event and have unacceptable LDL-cholesterol levels despite intensive statin treatment, PCSK9 inhibitors should be considered.

PMID: 31092149

## **Milk and Dairy Product Consumption and Cardiovascular Diseases: An Overview of Systematic Reviews and Meta-Analyses.**

Fontecha J, Calvo MV, Juarez M, Gil A, Martínez-Vizcaino V.

Milk and dairy products containing milk fat are major food sources of saturated fatty acids, which have been linked to increased risk of cardiovascular-related clinical outcomes such as cardiovascular disease (CVD), coronary heart disease (CHD), and stroke. Therefore, current recommendations by health authorities advise consumption of low-fat or fat-free milk. Today, these recommendations are seriously questioned by meta-analyses of both prospective cohort studies and randomized controlled trials (RCTs) reporting inconsistent results. The present study includes an overview of systematic reviews and meta-analyses of follow-up studies, an overview of meta-analyses involving RCTs, and an update on meta-analyses of RCTs (2013-2018) aiming to synthesize the evidence regarding the influence of dairy product consumption on the risk of major cardiovascular-related outcomes and how various doses of different dairy products affect the responses, as well as on selected biomarkers of cardiovascular disease risk, i.e., blood pressure and blood lipids. The search strategies for both designs were conducted in the MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, and Web of Science databases from their inception to April 2018. From the 31 full-text articles retrieved for cohort studies, 17 met the eligibility criteria. The pooled risk ratio estimated for the association between the consumption of different dairy products at different dose-responses and cardiovascular outcomes (CVD, CHD, and stroke) showed a statistically significant negative association with RR values  $<1$ , or did not find evidence of significant association. The overview of 12 meta-analyses involving RCTs as well as the updated meta-analyses of RCTs did not result in significant changes on risk biomarkers such as systolic and diastolic blood pressure and total cholesterol and LDL cholesterol. Therefore, the present study states that the consumption of total dairy products, with either regular or low fat content, does not adversely affect the risk of CVD.

PMID: 31089735

## **BMI, Mortality, and Cardiovascular Outcomes in Type 1 Diabetes: Findings Against an Obesity Paradox.**

Edqvist J, Rawshani A, Adiels M, Björck L, Lind M, Svensson AM, Gudbjörnsdóttir S, Sattar N, Rosengren A.

**OBJECTIVE:** Low weight has been associated with increased mortality risks in type 1 diabetes. We aimed to investigate the importance of weight and weight gain/loss in the Swedish population diagnosed with type 1 diabetes.

**RESEARCH DESIGN AND METHODS:** Patients with type 1 diabetes (n = 26,125; mean age 33.3 years; 45% women) registered in the Swedish National Diabetes Registry from 1998 to 2012 were followed from the first day of study entry. Cox regression was used to calculate risk of death from cardiovascular disease (CVD), major CVD events, hospitalizations for heart failure (HF), and total deaths.

**RESULTS:** Population mean BMI in patients with type 1 diabetes increased from 24.7 to 25.7 kg/m<sup>2</sup> from 1998 to 2012. Over a median follow-up of 10.9 years, there were 1,031 deaths (33.2% from CVD), 1,460 major CVD events, and 580 hospitalizations for HF. After exclusion of smokers, patients with poor metabolic control, and patients with a short follow-up time, there was no increased risk for mortality in those with BMI <25 kg/m<sup>2</sup>, while BMI >25 kg/m<sup>2</sup> was associated with a minor increase in risk of mortality, major CVD, and HF. In women, associations with BMI were largely absent. Weight gain implied an increased risk of mortality and HF, while weight loss was not associated with higher risk.

**CONCLUSIONS:** Risk of major CVD, HF, CVD death, and mortality increased with increasing BMI, with associations more apparent in men than in women. After exclusion of factors associated with reverse causality, there was no evidence of an obesity paradox.

PMID: 31048408

## **Glucose-lowering therapy and cardiovascular outcomes in patients with type 2 diabetes mellitus and acute coronary syndrome.**

Avogaro A, Bonora E, Consoli A, Del Prato S, Genovese S, Giorgino F.

Diabetes is a common comorbidity in patients hospitalized for an acute coronary syndrome event, and prevalence is increasing. Among patients hospitalized with acute myocardial infarction, diabetes can be an independent predictor of mortality and new cardiovascular events; both short- and long-term outcomes are worse for patients with diabetes relative to those without, and undiagnosed diabetes is associated with greater mortality. The impact of glycemic control on cardiovascular outcomes and the best approach to treat hyperglycemia upon hospital admission for acute coronary syndrome in patients with or without known diabetes remain open questions. This review assesses available evidence for hyperglycemia management at the time of admission for acute coronary syndrome and, thereafter, finds that (1) admission plasma glucose plays a role in predicting adverse events, especially in patients with unknown diabetes; (2) glycosylated haemoglobin is a likely predictor of events in patients with unknown diabetes; and (3) hypoglycemia at the time of acute myocardial infarction hospital admission is an important predictor for mortality in patients with and without diabetes. Whether glucose-targeted insulin and glucose infusion have advantages over glucose-insulin-potassium infusion remains controversial. Evidence for the effect of novel glucose-lowering agents used at the time of an acute cardiovascular event is limited and requires more dedicated studies.

PMID: 31044622

## **Effect of ischemic preconditioning on cardiovascular outcomes in patients with symptomatic coronary artery disease: a cohort study.**

Rahmi RM, Hueb W, Rezende PC, Garzillo CL, Uchida AH, Scudeler TL, Ramires JAF, Filho RK.

**BACKGROUND:** Despite the powerful myocardial protection of ischemic preconditioning (IP) observed in experimental studies, it remains a challenge to observe such protection in humans. Thus, the aim of this study was to evaluate the possible effects of IP on clinical outcomes in patients with coronary artery disease (CAD).

**PATIENTS AND METHODS:** In this cohort study, patients with multivessel CAD, preserved systolic ventricular function, and stable angina were prospectively selected. They underwent two sequential exercise stress tests (EST) to evaluate IP presence. IP was considered present if patients had an improvement in the time to the onset of 1.0-mm ST-segment deviation in the second EST. The primary end point was the composite rate of cardiac death, nonfatal myocardial infarction, or revascularization during 1-year follow-up. Patients with (IP+) and without (IP-) the cardioprotective mechanism were compared regarding clinical end points.

**RESULTS:** A total of 229 patients completed EST and had IP evaluated: 165 (72%) were IP+ and 64 (28%) were IP- patients. Of these, 218 patients had complete follow-up. At 1-year, event-free survival regarding the primary end point was 95.5 versus 83.6% ( $P=0.0024$ ) and event-free survival regarding cardiac death or myocardial infarction was 99.4 versus 91.7% ( $P=0.0020$ ), respectively, in IP+ and IP- groups. The unadjusted hazard ratio (IP+/IP-) for the primary end point was 4.63 (1.52-14.08). After multivariate analysis, IP was still significantly associated with better clinical outcomes ( $P=0.0025$ ).

**CONCLUSION:** This data suggest that IP may contribute to better clinical outcomes in patients with ischemic heart disease.

PMID: 30994494



## **Neck circumference and cardiovascular outcomes: Insights from the Jackson Heart Study.**

Pumill CA, Bush CG, Greiner MA, Hall ME, Dunlay SM, Correa A, Curtis LH, Suzuki T, Hardy C, Blackshear CT, O'Brien EC, Mentz RJ.

**BACKGROUND:** Emerging data suggest that neck circumference (NC) is associated with cardiometabolic risk factors. Limited research is available regarding the association between NC and cardiovascular outcomes in African Americans.

**METHODS:** Using data from the Jackson Heart Study, we included participants with recorded NC measurements at baseline (2000-2004). Baseline characteristics for the included population were summarized by tertiles of NC. We then calculated age- and sex-adjusted cumulative incidence of clinical cardiovascular outcomes and performed Cox proportional-hazards with stepwise models.

**RESULTS:** Overall, 5,290 participants were categorized into tertiles of baseline NC defined as  $\leq 37$  cm ( $n = 2179$ ), 38-40 cm ( $n = 1552$ ), and  $>40$  cm ( $n = 1559$ ). After adjusting for age and sex, increasing NC was associated with increased risk of heart failure (HF) hospitalization (cumulative incidence = 13.4% [99% CI, 10.7-16.7] in the largest NC tertile vs 6.5% [99% CI, 4.7-8.8] in the smallest NC tertile), but not mortality, stroke, myocardial infarction, or coronary heart disease (all  $P \geq .1$ ). Following full risk adjustment, there was a nominal increase in the risk of HF hospitalization with increasing NC, but this was not statistically significant (hazard ratio per 1-cm increase, 1.04 [99% CI, 0.99-1.10],  $P = .06$ ).

**CONCLUSIONS:** In this large cohort of African American individuals, a larger NC was associated with increased risk for HF hospitalization following adjustment for age and sex, but this risk was not statistically significant after adjusting for other clinical variables. Although NC is not independently associated with increased risk for cardiovascular events, it may offer prognostic information particularly related to HF hospitalization.

PMID: 30954832

## **Albuminuria as a Predictor of Cardiovascular Outcomes in Patients With Acute Myocardial Infarction.**

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**Background** In patients with myocardial infarction ( MI ), reduced kidney function is recognized as an important predictor of poor prognosis, but the impact of albuminuria, a representative measure of kidney damage, has not been extensively evaluated. **Methods and Results** In the SCREAM (Stockholm Creatinine Measurements) project (2006-2012), we identified 2469 patients with incident MI with dipstick proteinuria measured within a year before MI (427 patients also had urine albumin to creatinine ratio [ ACR ] measured concurrently) and obtained estimates for ACR with multiple imputation in participants with data solely on dipstick proteinuria. We quantified the association of ACR with the post- MI composite and individual outcomes of all-cause mortality, cardiovascular mortality, recurrent MI , ischemic stroke, or heart failure using Cox models and then evaluated the improvement in C statistic. During a median follow-up of 1.0 year after MI , 1607 participants (65.1%) developed the post- MI composite outcome. Higher ACR levels were independently associated with all outcomes except for ischemic stroke. Per 8-fold higher ACR (eg, 40 versus 5 mg/g), the hazard ratio of composite outcome was 1.21 (95% CI , 1.08-1.35). The addition of the ACR improved the C statistic of the post- MI composite by 0.040 (95% CI, 0.030-0.051). Largely similar results were obtained regardless of diabetic status and when ACR or dipstick was separately analyzed without imputation. **Conclusions** In patients with MI , albuminuria was a potent predictor of subsequent outcomes, suggesting the importance of paying attention to the information on albuminuria, in addition to kidney function, in this high-risk population.

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