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J Am Coll Cardiol. 2017 Dec 19;70(24):2979-2991.

Normal LDL-Cholesterol Levels Are Associated With Subclinical Atherosclerosis in the Absence of Risk Factors.

Fernández-Friera L, Fuster V, López-Melgar B, Oliva B, García-Ruiz JM, Mendiguren J, Bueno H, Pocock S, Ibáñez B, Fernández-Ortiz A, Sanz J.

BACKGROUND: Absence of cardiovascular risk factors (CVRFs) is traditionally considered low risk for atherosclerosis; however, individuals without CVRFs, as currently defined, still have events.
OBJECTIVES: This study sought to identify predictors of subclinical atherosclerosis in CVRF-free individuals.
METHODS: Participants from the PESA (Progression of Early Subclinical Atherosclerosis) study (n = 4,184) without conventional CVRFs were evaluated (n = 1,779; 45.0 ± 4.1 years, 50.3% women). CVRF freedom was defined as no current smoking and untreated blood pressure <140/90 mm Hg, fasting glucose <126 mg/dl, total cholesterol <240 mg/dl, low-density lipoprotein cholesterol (LDL-C) <160 mg/dl, and high-density lipoprotein cholesterol ≥40 mg/dl. A subgroup with optimal CVRFs (n = 740) was also defined as having blood pressure <120/80 mm Hg, fasting glucose <100 mg/dl, glycosylated hemoglobin <5.7%, and total cholesterol <200 mg/dl. We evaluated ultrasound-detected carotid, iliofemoral, and abdominal aortic plaques; coronary artery calcification; serum biomarkers; and lifestyle. Adjusted odds ratios (with 95% confidence interval) and ordinal logistic regression models were used.
RESULTS: Subclinical atherosclerosis (plaque or coronary artery calcification) was present in 49.7% of CVRF-free participants. Together with male sex and age, LDL-C was independently associated with atherosclerosis presence and extent, in both the CVRF-free and CVRF-optimal groups (odds ratio [×10 mg/dl]: 1.14 to 1.18; p < 0.01 for all). Atherosclerosis presence and extent was also associated in the CVRF-free group with glycosylated hemoglobin levels.
CONCLUSIONS: Many CVRF-free middle-aged individuals have atherosclerosis. LDL-C, even at levels currently considered normal, is independently associated with the presence and extent of early systemic atherosclerosis in the absence of major CVRFs. These findings support more effective LDL-C lowering for primordial prevention, even in individuals conventionally considered at optimal risk. (Progression of Early Subclinical Atherosclerosis [PESA] Study; NCT01410318).

DOI: 10.1016/j.jacc.2017.10.024
PMID: 29241485

Am Heart J. 2017 Dec; 194:25-38.

Contemporary rates and correlates of statin use and adherence in nondiabetic adults with cardiovascular risk factors: The KP CHAMP study.

Go AS, Fan D, Sung SH, Inveiss AI, Romo-LeTourneau V, Mallya UG, Boklage S, Lo JC.

BACKGROUND: Statin therapy is highly efficacious in the prevention of fatal and nonfatal atherosclerotic events in persons at increased cardiovascular risk. However, its long-term effectiveness in practice depends on a high level of medication adherence by patients.
METHODS: We identified nondiabetic adults with cardiovascular risk factors between 2008 and 2010 within a large integrated health care delivery system in Northern California. Through 2013, we examined the use and adherence of newly initiated statin therapy based on data from dispensed prescriptions from outpatient pharmacy databases.
RESULTS: Among 209,704 eligible adults, 68,085 (32.5%) initiated statin therapy during the follow-up period, with 90.4% receiving low-potency statins. At 12 and 24 months after initiating statins, 84.3% and 80.2%, respectively, were actively receiving statin therapy, but only 42% and 30%, respectively, had no gaps in treatment during those time periods. There was also minimal switching between statins or use of other lipid-lowering therapies for augmentation during follow-up. Age≥50 years, Asian/Pacific Islander race, Hispanic ethnicity, prior myocardial infarction, prior ischemic stroke, hypertension, and baseline low-density lipoprotein cholesterol>100 mg/dL were associated with higher adjusted odds, whereas female gender, black race, current smoking, dementia were associated with lower adjusted odds, of active statin treatment at 12 months after initiation.
CONCLUSIONS: There remain opportunities for improving prevention in patients at risk for cardiovascular events. Our study identified certain patient subgroups that may benefit from interventions to enhance medication adherence, particularly by minimizing treatment gaps and discontinuation of statin therapy within the first year of treatment.

DOI: 10.1016/j.ahj.2017.08.013
PMID: 29223433

PLoS One. 2017 Dec 7; 12(12):e0189047

Longer time to peak glucose during the oral glucose tolerance test increases cardiovascular risk score and diabetes prevalence.

Lin YC, Chen HS.

INTRODUCTION: The pattern of glucose levels during an oral glucose tolerance test (OGTT) may be useful for predicting diabetes or cardiovascular disease (CVD). Our aim was to determine whether the time to peak glucose during the OGTT is associated with CVD risk scores and diabetes.

METHODS: Individuals with impaired fasting glucose (IFG) were enrolled in this observational study. Participants were grouped by the measured time to peak glucose (30, 60, 90 and 120 min) during the 75g OGTT. The primary outcome was 10-year CVD risk scores (using the Framingham risk score calculator). Secondary outcomes evaluated effect of time to peak glucose on prevalence of diabetes and indicators of glucose homeostasis.

RESULTS: A total of 125 patients with IFG underwent OGTTs. Framingham 10-year risk score for the 90-min group was 1.7 times higher than for the 60-min group (6.98±6.56% vs. 4.05±4.60%, P = 0.023). Based on multivariate linear regression, time to peak glucose at 90 min was associated with a higher Framingham risk score than 60-min group (β coefficient: 2.043, 95% confidence interval: 0.067-6.008, P = 0.045). The percentages of patients with HbA1c ≥6.5%, isolated post-challenge hyperglycemia (IPH) and diabetes (combined IPH and HbA1c ≥6.5%) were significantly increased with longer times to peak glucose. Prevalence of diabetes was higher in the 90-min group than in the 60-min group (31.5% vs. 5.7%, P = 0.001).

CONCLUSIONS: In subjects with IFG, those with a longer time to peak glucose had a higher Framingham 10-year risk score and were associated with a greater likelihood of IPH and diabetes.

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PMID: 29216249

PLoS Med. 2017 Dec 6; 14(12):e1002459.

Psychosocial and socioeconomic determinants of cardiovascular mortality in Eastern Europe: A multicentre prospective cohort study.

Tillmann T, Pikhart H, Peasey A, Kubinova R, Pajak A, Tamosiunas A, Malyutina S, Steptoe A, Kivimäki M, Marmot M, Bobak M.

BACKGROUND: Eastern European countries have some of the highest rates of cardiovascular disease (CVD) mortality, much of which cannot be adequately accounted for by conventional CVD risk factors. Psychosocial and socioeconomic factors may affect risk of CVD, but relatively few studies on this issue have been undertaken in Eastern Europe. We investigated whether various psychosocial factors are associated with CVD mortality independently from each other and whether they can help explain differences in CVD mortality between Eastern European populations.

METHODS: Participants were from the Health, Alcohol and Psychological factors in Eastern Europe (HAPIEE) cohort study in Russia, Poland and the Czech Republic, including a total of 20,867 men and women aged 43-74 years and free of CVD at baseline examination during 2002-2005. Participants were followed-up for CVD mortality after linkage to national mortality registries for a median of 7.2 years.

RESULTS: During the follow-up, 556 participants died from CVD. After mutual adjustment, six psychosocial and socioeconomic factors were associated with increased risk of CVD death: unemployment, low material amenities, depression, being single, infrequent contacts with friends or relatives. The hazard ratios [HRs] for these six factors ranged between 1.26 [95% confidence interval 1.14-1.40] and 1.81 [95% confidence interval 1.24-2.64], fully adjusted for each other, and conventional cardiovascular risk factors. Population-attributable fractions ranged from 8% [4%-13%] to 22% [11%-31%] for each factor, when measured on average across the three cohorts. However, the prevalence of psychosocial and socioeconomic risk factors and their HRs were similar between the three countries. Altogether, these factors could not explain why participants from Russia had higher CVD mortality when compared to participants from Poland/Czech Republic. Limitations of this study include measurement error that could lead to residual confounding; and the possibilities for reverse causation and/or unmeasured confounding from observational studies to lead to associations that are not causal in nature.

CONCLUSIONS: Six psychosocial and socioeconomic factors were associated with cardiovascular mortality, independent of each other. Differences in mortality between cohorts from Russia versus Poland or Check Republic remained unexplained.

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PMID: 29211726

Am J Med Sci. 2017 Dec; 354 (6):565-572.

Socioeconomic, Psychosocial and Behavioral Characteristics of Patients Hospitalized With Cardiovascular Disease.

Dupre ME, Nelson A, Lynch SM, Granger BB, Xu H, Churchill E, Willis JM, Curtis LH, Peterson ED.

BACKGROUND: Recent studies have drawn attention to nonclinical factors to better understand disparities in the development, treatment and prognosis of patients with cardiovascular disease. However, there has been limited research describing the nonclinical characteristics of patients hospitalized for cardiovascular care.

METHODS: Data for this study come from 520 patients admitted to the Duke Heart Center from January 1, 2015 through January 10, 2017. Electronic medical records and a standardized survey administered before discharge were used to ascertain detailed information on patients' demographic (age, sex, race, marital status and living arrangement), socioeconomic (education, employment and health insurance), psychosocial (health literacy, health self-efficacy, social support, stress and depressive symptoms) and behavioral (smoking, drinking and medication adherence) attributes.

RESULTS: Study participants were of a median age of 65 years, predominantly male (61.4%), non-Hispanic white (67.1%), hospitalized for 5.11 days and comparable to all patients admitted during this period. Results from the survey showed significant heterogeneity among patients in their demographic, socioeconomic and behavioral characteristics. We also found that the patients' levels of psychosocial risks and resources were significantly associated with many of these nonclinical characteristics. Patients who were older, women, nonwhite and unmarried had generally lower levels of health literacy, self-efficacy and social support, and higher levels of stress and depressive symptoms than their counterparts.

CONCLUSIONS: Patients hospitalized with cardiovascular disease have diverse nonclinical profiles that have important implications for targeting interventions. A better understanding of these characteristics will enhance the personalized delivery of care and improve outcomes in vulnerable patient groups.

DOI: 10.1016/j.amjms.2017.07.011
PMID: 29208253

J Am Coll Cardiol. 2017 Dec 5;70(22):2739-2749.

Abdominal Obesity Is Associated With an Increased Risk of All-Cause Mortality in Patients With HFpEF.

Tsujimoto T, Kajio H.

BACKGROUND: There is a lack of studies that evaluate the association between abdominal obesity and subsequent outcomes in patients with heart failure with preserved ejection fraction (HFpEF).
OBJECTIVES: The present study aimed to assess the association between abdominal obesity and risk of all-cause mortality in patients with HFpEF. METHODS: The present study used data from the TOPCAT (Treatment of Preserved Cardiac Function Heart Failure with an Aldosterone Antagonist) trial. The primary outcome was all-cause mortality. We analyzed and compared the hazard ratios (HRs) in patients with abdominal obesity and those without abdominal obesity using multivariable Cox proportional hazard models. Abdominal obesity was defined as a waist circumference of ≥102 cm in men and ≥88 cm in women.
RESULTS: The present study included 3,310 patients with HFpEF: 2,413 patients with abdominal obesity and 897 without abdominal obesity. The mean follow-up was 3.4 ± 1.7 years. During follow-up, 500 patients died. All-cause mortality rates in patients with and without abdominal obesity were 46.1 and 40.7 events per 1,000 person-years, respectively. After multivariable adjustment, the risk of all-cause mortality was significantly higher in patients with abdominal obesity than in those without abdominal obesity (adjusted HR: 1.52; 95% confidence interval [CI]: 1.16 to 1.99; p = 0.002). The risk of cardiovascular and noncardiovascular mortality was also significantly higher in patients with abdominal obesity than in those without abdominal obesity (adjusted HR: 1.50; 95% CI: 1.08 to 2.08; p = 0.01 and adjusted HR: 1.58; 95% CI: 1.00 to 2.51; p = 0.04, respectively).
CONCLUSIONS: The risk of all-cause mortality was significantly higher in patients with HFpEF with abdominal obesity than in those without abdominal obesity.

DOI: 10.1016/j.jacc.2017.09.1111
PMID: 29191321

PLoS One. 2017 Nov 29;12(11):e0187923.

Breastfeeding and maternal cardiovascular risk factors and outcomes: A systematic review.

Nguyen B, Jin K, Ding D.

BACKGROUND: There is growing evidence that breastfeeding has short- and long-term cardiovascular health benefits for mothers. The objectives of this systematic review were to examine the association between breastfeeding and maternal cardiovascular risk factors and outcomes that have not previously been synthesized systematically, including metabolic syndrome, hypertension and cardiovascular disease.

METHODS AND FINDINGS: This systematic review meets PRISMA guidelines. The MEDLINE, EMBASE and CINAHL databases were systematically searched for relevant publications of any study design from the earliest publication date to March 2016. The reference lists from selected articles were reviewed, and forward and backward referencing were conducted. The methodological quality of reviewed articles was appraised using validated checklists. Twenty-one studies meeting the inclusion criteria examined the association between self-reported breastfeeding and one or more of the following outcomes: metabolic syndrome/metabolic risk factors (n = 10), inflammatory markers/adipokines (n = 2), hypertension (n = 7), subclinical cardiovascular disease (n = 2), prevalence/incidence of cardiovascular disease (n = 3) and cardiovascular disease mortality (n = 2). Overall, 19 studies (10 cross-sectional/retrospective, 9 prospective) reported significant protective effects of breastfeeding, nine studies (3 cross-sectional/retrospective, 5 prospective, 1 cluster randomized controlled trial) reported non-significant findings and none reported detrimental effects of breastfeeding. In most studies reporting significant associations, breastfeeding remained associated with both short- and long-term maternal cardiovascular health risk factors/outcomes, even after covariate adjustment. Findings from several studies suggested that the effects of breastfeeding may diminish with age and a dose-response association between breastfeeding and several metabolic risk factors. However, further longitudinal studies, including studies that measure exclusive breastfeeding, are needed to confirm these findings.

CONCLUSIONS: The evidence from this review suggests that breastfeeding is associated with cardiovascular health benefits. However, results should be interpreted with caution as the evidence gathered for each individual outcome was limited by the small number of observational studies. Additional prospective studies are needed.

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PMID: 29186142

Nutr Metab Cardiovasc Dis. 2017 Dec;27(12):1060-1080.

A systematic review of the effect of dietary saturated and polyunsaturated fat on heart disease.

Clifton PM, Keogh JB.

AIMS: Over the last 7 years there has been intense debate about the advice to reduce saturated fat and increase polyunsaturated fat to reduce CVD risk. The aim of this review was to examine systematic reviews and meta-analyses since 2010 on this topic plus additional cohort studies and interventions not included in these reviews.
DATA SYNTHESIS: High saturated and trans fat intake (which elevates LDL like saturated fat) in the Nurses and Health Professional Follow-Up Studies combined is associated with an 8-13% higher mortality and replacement of saturated fat with any carbohydrate, PUFA and MUFA is associated with lower mortality with PUFA being more effective than MUFA (19% reduction versus 11%). With CVD mortality only PUFA and fish oil replacement of saturated fat lowers risk with a 28% reduction in CVD mortality per 5% of energy. Replacing saturated fat with PUFA or MUFA is equally effective at reducing CHD events and replacement with whole grains will lower events while replacement with sugar and starch increases events. Replacement of saturated fat with carbohydrate has no effect on CHD events or death. Only PUFA replacement of saturated fat lowers CHD events and CVD and total mortality. Replacing saturated fat with linoleic acid appears to be beneficial based on the Hooper Cochrane meta-analysis of interventions although other analyses with fewer studies have shown no effect.
CONCLUSIONS: Reducing saturated fat and replacing it with carbohydrate will not lower CHD events or CVD mortality although it will reduce total mortality. Replacing saturated fat with PUFA, MUFA or high-quality carbohydrate will lower CHD events.

DOI: 10.1016/j.numecd.2017.10.010
PMID: 29174025

J Pediatr. 2017 Dec; 191:152-157.

Persistent High Non-High-Density Lipoprotein Cholesterol in Early Childhood: A Latent Class Growth Model Analysis.

Albaum JM, Carsley S, Chen Y, Dai DWH, Lebovic G, McCrindle BW, Maguire JL, Parkin PC, Birken CS; TARGet Kids! Collaboration.

OBJECTIVES: To examine patterns of non-high-density lipoprotein (HDL) cholesterol in early childhood and identify factors associated with persistent high non-HDL cholesterol in healthy urban children.

STUDY DESIGN: We identified all children enrolled in a primary care practice-based research network called TARGet Kids! (The Applied Research Group for Kids) with ≥3 laboratory measurements of non-HDL cholesterol. Latent class growth model analysis was performed to identify distinct trajectory groups for non-HDL cholesterol. Trajectory groups were then categorized into "normal" vs "persistent-high" non-HDL cholesterol based on guideline cut-off values and logistic regression was completed to examine the association between trajectory group and the presence of anthropometric and cardiometabolic risk factors.

RESULTS: A total of 608 children met inclusion criteria for the trajectory analysis (median age at enrolment = 18.3, IQR = 27.9 months). Four trajectory groups were identified with 2 groups (n = 451) categorized as normal non-HDL cholesterol and 2 groups (n = 157) as persistent high non-HDL cholesterol. Family history of high cholesterol (OR 2.04, 95% CI 1.27-3.28) was associated significantly with persistent high non-HDL cholesterol, whereas East/Southeast Asian vs European ethnicity (OR 0.33, 95% CI 0.14-0.78), longer breastfeeding duration (OR 0.96, 95% CI 0.93-1.00), and greater birth weight (OR 0.69, 95% CI 0.48-1.00) were associated with lower odds of persistent high non-HDL cholesterol.

CONCLUSIONS: Patterns of non-HDL cholesterol are identified during early childhood, and family history of high cholesterol was associated most strongly with persistent high non-HDL cholesterol. Future research should inform the development of a clinical prediction tool for lipids in early childhood to identify children who may benefit from interventions to promote cardiovascular health.

DOI: 10.1016/j.jpeds.2017.08.079
PMID: 29173300

J Pediatr. 2017 Dec; 191:133-139.

Waist Circumference and Body Mass Index in Children with Chronic Kidney Disease and Metabolic, Cardiovascular, and Renal Outcomes.

Patel HP, Saland JM, Ng DK, Jiang S, Warady BA, Furth SL, Flynn JT.

OBJECTIVE: To describe the prevalence of obesity as estimated by waist circumference (WC) and body mass index (BMI) and compare associations of WC and BMI with indicators of metabolic, cardiovascular, and renal health in children with chronic kidney disease (CKD).

STUDY DESIGN: Cross-sectional analysis stratified by CKD etiology (nonglomerular or glomerular) of 737 subjects. The kappa statistic was used to assess agreement between the 2 measures of obesity. Linear regression models were performed using WC and BMI as separate independent variables. Dependent variables included lipid measures, insulin resistance, blood pressure, left ventricular mass index, proteinuria, and estimated glomerular filtration rate. Associations were scaled to SD and interpreted as the change in dependent variable associated with a 1-SD change in WC or BMI.

RESULTS: There was good agreement (kappa statistic=0.68) between WC and BMI in identifying obesity. Approximately 10% of subjects had obesity by 1 measure but not the other. BMI was more strongly associated with estimated glomerular filtration rate than WC. BMI was more strongly associated with left ventricular mass index in the nonglomerular CKD group compared with WC, but both had significant associations. The associations between WC and BMI with the remainder of the dependent variables were not significantly different.

CONCLUSIONS: Measurement of WC added limited information to BMI in this cohort. Further longitudinal study is needed to determine how WC and BMI compare in predicting outcomes, particularly for children with CKD identified as having obesity by 1 measure but not the other.

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PMCID: PMC5728693 [Available on 2018-12-01]
PMID: 29173296

Nutr Metab Cardiovasc Dis. 2017 Dec;27(12):1130-1135.

The association between muscle mass deficits and arterial stiffness in middle-aged men.

Im IJ, Choi HJ, Jeong SM, Kim HJ, Son JS, Oh HJ.

BACKGROUND AND AIMS: Early diagnosis of arteriosclerosis is fundamental for the prevention of cardiovascular morbidity and mortality. The current study was performed to identify major predictors of arteriosclerosis and to assess the association between arterial stiffness as measured by cardio-ankle vascular index (CAVI) and muscle mass deficit (MMD) estimated by bioelectrical impedance analysis (BIA) in middle-aged men.

METHODS AND RESULTS: Data were gathered from 3356 middle-aged men who visited a health promotion center. CAVI was measured as an index of arterial stiffness. Body composition analysis was performed using BIA. MMD was positively associated with CAVI in the regression model. The odds ratios for high-CAVI (≥9.0) rose with MMD grade in a dose-dependent manner after adjusting for age, lifestyle factors and current medication use. The estimated mean CAVI rose as MMD grade increased (P for trend >0.001).

CONCLUSIONS: MMD estimated from BIA was positively associated with arterial stiffness in middle-aged men. These findings show a close interaction between low muscle mass and cardiovascular risk.

DOI: 10.1016/j.numecd.2017.10.002
PMID: 29170061

Nutr Metab Cardiovasc Dis. 2017 Dec;27(12):1143-1151.

Low vitamin D status in relation to cardiovascular disease and mortality in Swedish women - Effect of extended follow-up.

Leu Agelii M, Lehtinen-Jacks S, Zetterberg H, Sundh V, Björkelund C, Lissner L.

BACKGROUND AND AIMS: The impact of vitamin D concentrations on subsequent cardiovascular disease (CVD) and overall mortality has been generally examined for periods under two decades. The magnitude of the association may depend on follow-up length. We aimed to investigate the relationship between baseline vitamin D and risk of total CVD, stroke and all-cause mortality over three decades of follow-up. Secondly, we aimed to assess how follow-up affects the associations.
METHODS AND RESULTS: Concentrations of 25-hydroxyvitamin D (25D) were measured in a population-based sample of 1227 middle-aged women using serum collected at baseline and categorized into low (lowest 25D quartile) vs high 25D status (upper three 25D quartiles). Hazard ratio (HR) of the endpoints was estimated for low 25D. The impact of follow-up was examined in intermediary analyses where follow-up was interrupted up to four times, each time decreasing it by five years. There were 596 cardiovascular events and 635 participants died. During the first 17 years, the low 25D group experienced a 29% higher CVD risk and 3.3-fold higher stroke risk after accounting for confounders. Longer follow-up diminished significantly these risks and 25D status had no contribution at 32 years. For mortality, the decline over time was less dramatic, with HR = 1.96 (1.25; 3.08) at 17 years and HR = 1.42 (1.17; 1.72) at 37 years.
CONCLUSION: Low 25D status increased the risk for all endpoints, but a lengthy follow-up diminished these risks towards the null. The impact of follow-up depends on the outcome. Future studies of 25D and disease should use repeated 25D assessments.

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PMID: 29170060

BMC Med Genet. 2017 Nov 21;18(1):138.

Association of common genetic variants related to atrial fibrillation and the risk of ventricular fibrillation in the setting of first ST-elevation myocardial infarction.

Jabbari R, Jabbari J, Glinge C, Risgaard B, Sattler S, Winkel BG, Terkelsen CJ, Tilsted HH, Jensen LO, Hougaard M, Haunsø S, Engstrøm T, Albert CM, Tfelt-Hansen J.

BACKGROUND: Cohort studies have revealed an increased risk for ventricular fibrillation (VF) and sudden cardiac death (SCD) in patients with atrial fibrillation (AF). In this study, we hypothesized that single nucleotide polymorphisms (SNP) previously associated with AF may be associated with the risk of VF caused by first ST-segment elevation myocardial infarction (STEMI).
METHODS: We investigated association of 24 AF-associated SNPs with VF in the prospectively assembled case-control study among first STEMI-patients of Danish ancestry.
RESULTS: We included 257 cases (STEMI with VF) and 537 controls (STEMI without VF). The median age at index infarction was 60 years for the cases and 61 years for the controls ($p=0.100$). Compared to the control group, the case group was more likely to be male (86% vs. 75%, $p=0.001$), have a history of AF (7% vs. 2%, $p=0.006$) or hypercholesterolemia (39% vs. 31%, $p=0.023$), and a family history of sudden death (40% vs. 25%, $p<0.001$). All 24 selected SNPs have previously been associated with AF. None of the 24 SNPs were associated with the risk of VF after adjustment for age and sex under additive genetic model of inheritance in the logistic regression model.
CONCLUSION: In this study, we found that the 24 AF-associated SNPs may not be involved in increasing the risk of VF. Larger VF cohorts and use of new next generation sequencing and epigenetic may in future identify additional AF and VF risk loci and improve our understanding of genetic pathways behind the two arrhythmias.

DOI: 10.1186/s12881-017-0497-1
PMCID: PMC5699191
PMID: 29162046

BMJ. 2017 Nov 20;359:j5019.

Development and validation of QDiabetes-2018 risk prediction algorithm to estimate future risk of type 2 diabetes: cohort study.

Hippisley-Cox J, Coupland C.

Objectives To derive and validate updated QDiabetes-2018 prediction algorithms to estimate the 10 year risk of type 2 diabetes in men and women, taking account of potential new risk factors, and to compare their performance with current approaches.Design Prospective open cohort study.Setting Routinely collected data from 1457 general practices in England contributing to the QResearch database: 1094 were used to develop the scores and a separate set of 363 were used to validate the scores.Participants 11.5 million people aged 25-84 and free of diabetes at baseline: 8.87 million in the derivation cohort and 2.63 million in the validation cohort.Methods Cox proportional hazards models were used in the derivation cohort to derive separate risk equations in men and women for evaluation at 10 years. Risk factors considered included those already in QDiabetes (age, ethnicity, deprivation, body mass index, smoking, family history of diabetes in a first degree relative, cardiovascular disease, treated hypertension, and regular use of corticosteroids) and new risk factors: atypical antipsychotics, statins, schizophrenia or bipolar affective disorder, learning disability, gestational diabetes, and polycystic ovary syndrome. Additional models included fasting blood glucose and glycated haemoglobin (HBA1c). Measures of calibration and discrimination were determined in the validation cohort for men and women separately and for individual subgroups by age group, ethnicity, and baseline disease status. Main outcome measure Incident type 2 diabetes recorded on the general practice record. Results In the derivation cohort, 178314 incident cases of type 2 diabetes were identified during follow-up arising from 42.72 million person years of observation. In the validation cohort, 62326 incident cases of type 2 diabetes were identified from 14.32 million person years of observation. All new risk factors considered met our model inclusion criteria. Model A included age, ethnicity, deprivation, body mass index, smoking, family history of diabetes in a first degree relative, cardiovascular disease, treated hypertension, and regular use of corticosteroids, and new risk factors: atypical antipsychotics, statins, schizophrenia or bipolar affective disorder, learning disability, and gestational diabetes and polycystic ovary syndrome in women. Model B included the same variables as model A plus fasting blood glucose. Model C included HBA1c instead of fasting blood glucose. All three models had good calibration and high levels of explained variation and discrimination. In women, model B explained 63.3% of the variation in time to diagnosis of type 2 diabetes (R2), the D statistic was 2.69 and the Harrell's C statistic value was 0.89. The corresponding values for men were 58.4%, 2.42, and 0.87. Model B also had the highest sensitivity compared with current recommended practice in the National Health Service based on bands of either fasting blood glucose or HBA1c. However, only 16% of patients had complete data for blood

glucose measurements, smoking, and body mass index. Conclusions Three updated QDiabetes risk models to quantify the absolute risk of type 2 diabetes were developed and validated: model A does not require a blood test and can be used to identify patients for fasting blood glucose (model B) or HBA1c (model C) testing. Model B had the best performance for predicting 10 year risk of type 2 diabetes to identify those who need interventions and more intensive follow-up, improving on current approaches. Additional external validation of models B and C in datasets with more completely collected data on blood glucose would be valuable before the models are used in clinical practice.

PMCID: PMC5694979
PMID: 29158232

Mayo Clin Proc. 2017 Dec;92(12):1763-1771.

Moderate to High Levels of Cardiorespiratory Fitness Attenuate the Effects of Triglyceride to High-Density Lipoprotein Cholesterol Ratio on Coronary Heart Disease Mortality in Men.

Farrell SW, Finley CE, Barlow CE, Willis BL, DeFina LF, Haskell WL, Vega GL.

OBJECTIVE: To examine the prospective relationships among cardiorespiratory fitness (CRF), fasting blood triglyceride to high density lipoprotein cholesterol ratio (TG:HDL-C), and coronary heart disease (CHD) mortality in men.

METHODS: A total of 40,269 men received a comprehensive baseline clinical examination between January 1, 1978, and December 31, 2010. Their CRF was determined from a maximal treadmill exercise test. Participants were divided into CRF categories of low, moderate, and high fit by age group and by TG:HDL-C quartiles. Hazard ratios for CHD mortality were computed using Cox regression analysis.

RESULTS: A total of 556 deaths due to CHD occurred during a mean ± SD of 16.6±9.7 years (669,678 man-years) of follow-up. A significant positive trend in adjusted CHD mortality was shown across decreasing CRF categories (P for trend<.01). Adjusted hazard ratios were significantly higher across increasing TG:HDL-C quartiles as well (P for trend<.01). When grouped by CRF category and TG:HDL-C quartile, there was a significant positive trend (P=.04) in CHD mortality across decreasing CRF categories in each TG:HDL-C quartile.

CONCLUSION: Both CRF and TG:HDL-C are significantly associated with CHD mortality in men. The risk of CHD mortality in each TG:HDL-C quartile was significantly attenuated in men with moderate to high CRF compared with men with low CRF. These results suggest that assessment of CRF and TG: HDL-C should be included for routine CHD mortality risk assessment and risk management.

DOI: 10.1016/j.mayocp.2017.08.015
PMID: 29157534

PLoS Med. 2017 Nov 17;14 (11):e1002445.

Postmenopausal hormone therapy and risk of stroke: A pooled analysis of data from population-based cohort studies.

Carrasquilla GD, Frumento P, Berglund A, Borgfeldt C, Bottai M, Chiavenna C, Eliasson M, Engström G, Hallmans G, Jansson JH, Magnusson PK, Nilsson PM, Pedersen NL, Wolk A, Leander K.

BACKGROUND: Recent research indicates a favourable influence of postmenopausal hormone therapy (HT) if initiated early, but not late, on subclinical atherosclerosis. However, the clinical relevance of timing of HT initiation for hard end points such as stroke remains to be determined. Further, no previous research has considered the timing of initiation of HT in relation to haemorrhagic stroke risk. The importance of the route of administration, type, active ingredient, and duration of HT for stroke risk is also unclear. We aimed to assess the association between HT and risk of stroke, considering the timing of initiation, route of administration, type, active ingredient, and duration of HT.

METHODS AND FINDINGS: Data on HT use reported by the participants in 5 population-based Swedish cohort studies, with baseline investigations performed during the period 1987-2002, were combined in this observational study. In total, 88,914 postmenopausal women who reported data on HT use and had no previous cardiovascular disease diagnosis were included. Incident events of stroke (ischaemic, haemorrhagic, or unspecified) and haemorrhagic stroke were identified from national population registers. Laplace regression was employed to assess crude and multivariable-adjusted associations between HT and stroke risk by estimating percentile differences (PDs) with 95% confidence intervals (CIs). The fifth and first PDs were calculated for stroke and haemorrhagic stroke, respectively. Crude models were adjusted for age at baseline only. The final adjusted models included age at baseline, level of education, smoking status, body mass index, level of physical activity, and age at menopause onset. Additional variables evaluated for potential confounding were type of menopause, parity, use of oral contraceptives, alcohol consumption, hypertension, dyslipidaemia, diabetes, family history of cardiovascular disease, and cohort. During a median follow-up of 14.3 years, 6,371 first-time stroke events were recorded; of these, 1,080 were haemorrhagic. Following multivariable adjustment, early initiation (<5 years since menopause onset) of HT was associated with a longer stroke-free period than never use (fifth PD, 1.00 years; 95% CI 0.42 to 1.57), but there was no significant extension to the time period free of haemorrhagic stroke (first PD, 1.52 years; 95% CI -0.32 to 3.37). When considering timing as a continuous variable, the stroke-free and the haemorrhagic stroke-free periods were maximal if HT was initiated approximately 0-5 years from the onset of menopause. If single conjugated equine oestrogen HT was used, late initiation of HT was associated with a shorter stroke-free (fifth PD, -4.41 years; 95% CI -7.14 to -1.68) and haemorrhagic stroke-free (first PD, -9.51 years; 95% CI -12.77 to -6.24)

period than never use. Combined HT when initiated late was significantly associated with a shorter haemorrhagic stroke-free period (first PD, -1.97 years; 95% CI -3.81 to -0.13), but not with a shorter stroke-free period (fifth PD, -1.21 years; 95% CI -3.11 to 0.68) than never use. Given the observational nature of this study, the possibility of uncontrolled confounding cannot be excluded. Further, immortal time bias, also related to the observational design, cannot be ruled out. CONCLUSIONS: When initiated early in relation to menopause onset, HT was not associated with increased risk of incident stroke, regardless of the route of administration, type of HT, active ingredient, and duration. Generally, these findings held also for haemorrhagic stroke. Our results suggest that the initiation of HT 0-5 years after menopause onset, as compared to never use, is associated with a decreased risk of stroke and haemorrhagic stroke. Late initiation was associated with elevated risks of stroke and haemorrhagic stroke when conjugated equine oestrogen was used as single therapy. Late initiation of combined HT was associated with haemorrhagic stroke risk.

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Nut Consumption and Risk of Cardiovascular Disease.

Guasch-Ferré M, Liu X, Malik VS, Sun Q, Willett WC, Manson JE, Rexrode KM, Li Y, Hu FB, Bhupathiraju SN.

BACKGROUND: The associations between specific types of nuts, specifically peanuts and walnuts, and cardiovascular disease remain unclear.
OBJECTIVES: The authors sought to analyze the associations between the intake of total and specific types of nuts and cardiovascular disease, coronary heart disease, and stroke risk.
METHODS: The authors included 76,364 women from the Nurses' Health Study (1980 to 2012), 92,946 women from the Nurses' Health Study II (1991 to 2013), and 41,526 men from the Health Professionals Follow-Up Study (1986 to 2012) who were free of cancer, heart disease, and stroke at baseline. Nut consumption was assessed using food frequency questionnaires at baseline and was updated every 4 years.
RESULTS: During 5,063,439 person-years of follow-up, the authors documented 14,136 incident cardiovascular disease cases, including 8,390 coronary heart disease cases and 5,910 stroke cases. Total nut consumption was inversely associated with total cardiovascular disease and coronary heart disease after adjustment for cardiovascular risk factors. The pooled multivariable hazard ratios for cardiovascular disease and coronary heart disease among participants who consumed 1 serving of nuts (28 g) 5 or more times per week, compared with the reference category (never or almost never), were 0.86 (95% confidence interval: 0.79 to 0.93; p for trend = 0.0002) and 0.80 (95% confidence interval: 0.72 to 0.89; p for trend <0.001), respectively. Consumption of peanuts and tree nuts (2 or more times/week) and walnuts (1 or more times/week) was associated with a 13% to 19% lower risk of total cardiovascular disease and 15% to 23% lower risk of coronary heart disease.
CONCLUSIONS: In 3 large prospective cohort studies, higher consumption of total and specific types of nuts was inversely associated with total cardiovascular disease and coronary heart disease.

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PMID: 29145952

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Predicting Subclinical Atherosclerosis in Low-Risk Individuals: Ideal Cardiovascular Health Score and Fuster-BEWAT Score.

Fernández-Alvira JM, Fuster V, Pocock S, Sanz J, Fernández-Friera L, Laclaustra M, Fernández-Jiménez R, Mendiguren J, Fernández-Ortiz A, Ibáñez B, Bueno H.

BACKGROUND: The ideal cardiovascular health score (ICHS) is recommended for use in primary prevention. Simpler tools not requiring laboratory tests, such as the Fuster-BEWAT (blood pressure [B], exercise [E], weight [W], alimentation [A], and tobacco [T]) score (FBS), are also available.
OBJECTIVES: The purpose of this study was to compare the effectiveness of ICHS and FBS in predicting the presence and extent of subclinical atherosclerosis.
METHODS: A total of 3,983 participants 40 to 54 years of age were enrolled in the PESA (Progression of Early Subclinical Atherosclerosis) cohort. Subclinical atherosclerosis was measured in right and left carotids, abdominal aorta, right and left iliofemoral arteries, and coronary arteries. Subjects were classified as having poor, intermediate, or ideal cardiovascular health based on the number of favorable ICHS or FBS.
RESULTS: With poor ICHS and FBS as references, individuals with ideal ICHS and FBS showed lower adjusted odds of having atherosclerotic plaques (ICHS odds ratio [OR]: 0.41; 95% confidence interval [CI]: 0.31 to 0.55 vs. FBS OR: 0.49; 95% CI: 0.36 to 0.66), coronary artery calcium (CACS) ≥1 (CACS OR: 0.41; 95% CI: 0.28 to 0.60 vs. CACS OR: 0.53; 95% CI: 0.38 to 0.74), higher number of affected territories (OR: 0.32; 95% CI: 0.26 to 0.41 vs. OR: 0.39; 95% CI: 0.31 to 0.50), and higher CACS level (OR: 0.40; 95% CI: 0.28 to 0.58 vs. OR: 0.52; 95% CI: 0.38 to 0.72). Similar levels of significantly discriminating accuracy were found for ICHS and FBS with respect to the presence of plaques (C-statistic: 0.694; 95% CI: 0.678 to 0.711 vs. 0.692; 95% CI: 0.676 to 0.709, respectively) and for CACS ≥1 (C-statistic: 0.782; 95% CI: 0.765 to 0.800 vs. 0.780; 95% CI: 0.762 to 0.798, respectively).
CONCLUSIONS: Both scores predict the presence and extent of subclinical atherosclerosis with similar accuracy, highlighting the value of the FBS as a simpler and more affordable score for evaluating the risk of subclinical disease.

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Association between environmental noise and subjective symptoms related to cardiovascular diseases among elderly individuals in Japan.

Azuma K, Uchiyama I.

Noise in housing environments may increase the risk of cardiovascular diseases (CVDs); however, the most significant sources of noise among elderly individuals remain poorly understood. A nationwide cross-sectional study comprised of 6,181 elderly people (age ≥ 65 years) was conducted using a web-based self-reported questionnaire in 2014. Questions pertaining to CVD-related subjective symptoms within the past year addressed symptoms of chest pain, disturbances in pulse, acute impaired tongue movement, limb paralysis, and foot pain or numbness during walking. Questions concerning noise included awakening during the night due to noise, automobile, neighborhood, construction, railway, and aircraft noise. The multivariable analyses revealed that all symptoms were significantly associated with awakening during the night due to noise. Automobile, construction, railway, and aircraft noise were significantly associated with more CVD-related symptoms at nighttime than at daytime. Our results suggest that noise at nighttime is an important risk factor for CVDs. Although several different sources of environmental noise, including automobile, neighborhood, construction, railway, and aircraft noise were found to be significantly associated with CVD-related symptoms, the strongest association was observed for construction noise, followed by neighborhood and automobile noise. The adjusted odds ratios (95% confidence intervals) for construction noise at nighttime were 1.12 (1.06-1.19) with disturbances in pulse, 1.21 (1.08-1.35) in acute impaired tongue movement, 1.25 (1.15-1.36) in limb paralysis, and 1.19 (1.12-1.28) in foot pain or numbness during walking. The associations with railway and aircraft noise were found to be weaker than those with automobile, neighborhood, and construction noise. Our study suggests that CVD-related symptoms may exhibit a greater association with construction, neighborhood, and automobile noise than with railway and aircraft noise.

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Effects of a mixed berry beverage on cognitive functions and cardiometabolic risk markers; A randomized cross-over study in healthy older adults.

Nilsson A, Salo I, Plaza M, Björck I.

BACKGROUND: Berries and associated bioactive compounds, e.g. polyphenols and dietary fibre (DF), may have beneficial implications with respect to the metabolic syndrome, including also cognitive functions. The aim of this study was to evaluate effects on cognitive functions and cardiometabolic risk markers of 5 wk intervention with a mixture of berries, in healthy humans.
METHODS: Forty healthy subjects between 50-70 years old were provided a berry beverage based on a mixture of berries (150g blueberries, 50g blackcurrant, 50g elderberry, 50g lingonberries, 50g strawberry, and 100g tomatoes) or a control beverage, daily during 5 weeks in a randomized crossover design. The control beverage (water based) was matched with respect to monosaccharides, pH, and volume. Cognitive tests included tests of working memory capacity, selective attention, and psychomotor reaction time. Cardiometabolic test variables investigated were blood pressure, fasting blood concentrations of glucose, insulin, blood lipids, inflammatory markers, and markers of oxidative stress.
RESULTS: The daily amounts of total polyphenols and DF from the berry beverage were 795 mg and 11g, respectively. There were no polyphenols or DF in the control beverage. The berry intervention reduced total- and LDL cholesterol compared to baseline (both $P<0.05$), and in comparison to the control beverage ($P<0.005$ and $P<0.01$, respectively). The control beverage increased glucose concentrations ($P<0.01$) and tended to increase insulin concentrations ($P = 0.064$) from base line, and increased insulin concentrations in comparison to the berry beverage ($P<0.05$). Subjects performed better in the working memory test after the berry beverage compared to after the control beverage ($P<0.05$). No significant effects on the other test variables were observed.
CONCLUSIONS: The improvements in cardiometabolic risk markers and cognitive performance after the berry beverage suggest preventive potential of berries with respect to type 2 diabetes, cardiovascular disease, and associated cognitive decline. Possibly the polyphenols and DF contributed to the beneficial effects. TRIAL REGISTRATION: ClinicalTrials.gov: NCT01562392.

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PMID: 29141041

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Efficacy of Tai Chi and qigong for the prevention of stroke and stroke risk factors: A systematic review with meta-analysis.

Lauche R, Peng W, Ferguson C, Cramer H, Frawley J, Adams J, Sibbritt D.

BACKGROUND: This review aims to summarize the evidence of Tai Chi and qigong interventions for the primary prevention of stroke, including the effects on populations with major stroke risk factors.
METHODS: A systematic literature search was conducted on January 16, 2017 using the PubMed, Scopus, Cochrane Library, and CINAHL databases. Randomized controlled trials examining the efficacy of Tai Chi or qigong for stroke prevention and stroke risk factors were included. Risk of bias was assessed using the Cochrane Risk of Bias tool.
RESULTS: Twenty-one trials with n=1604 patients with hypertension, hyperlipidaemia, diabetes, overweight or obesity, or metabolic syndrome were included. No trials were found that examined the effects of Tai Chi/qigong on stroke incidence. Meta-analyses revealed significant, but not robust, benefits of Tai Chi/qigong over no interventions for hypertension (systolic blood pressure: -15.55mm Hg (95% CI: -21.16; -9.95); diastolic blood pressure: -10.66mm Hg (95% CI: -14.90, -6.43); the homeostatic model assessment (HOMA) index (-2.86%; 95% CI: -5.35, -0.38) and fasting blood glucose (-9.6mg/dL; 95% CI: -17.28, -1.91), and for the body mass index compared with exercise controls (-1.65kg/m; 95% CI: -3.11, -0.20). Risk of bias was unclear or high for the majority of trials and domains, and heterogeneity between trials was high. Only 6 trials adequately reported safety. No recommendation for the use of Tai Chi/qigong for the prevention of stroke can be given.
CONCLUSION: Although Tai Chi and qigong show some potential more robust studies are required to provide conclusive evidence on the efficacy and safety of Tai Chi and qigong for reducing major stroke risk factors.

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Association of metabolic syndrome and its components with all-cause and cardiovascular mortality in the elderly: A meta-analysis of prospective cohort studies.

Ju SY, Lee JY, Kim DH.

There is increasing evidence regarding the relationship between metabolic syndrome and mortality. However, previous research examining metabolic syndrome and mortality in older populations has produced mixed results. In addition, there is a clear need to identify and manage individual components of metabolic syndrome to decrease cardiovascular disease (CVD) mortality. In this meta-analysis, we searched the MEDLINE databases using PubMed, Cochrane Library, and EMBASE databases. Based on 20 prospective cohort studies, metabolic syndrome was associated with a higher risk of all-cause mortality [relative risk (RR), 1.23; 95% confidence interval (CI), 1.15-1.32; I=55.9%] and CVD mortality (RR, 1.24; 95% CI, 1.11-1.39; I=58.1%). The risk estimates of all-cause mortality for single components of metabolic syndrome were significant for higher values of waist circumference or body mass index (RR, 0.94; 95% CI, 0.88-1.00), higher values of blood glucose (RR, 1.19; 95% CI, 1.05-1.34), and lower values of high-density lipoprotein (HDL) cholesterol (RR, 1.11; 95% CI, 1.02-1.21). In the elderly population, metabolic syndrome was associated with an increased risk of all-cause and CVD mortality. Among the individual components of metabolic syndrome, increased blood glucose and HDL cholesterol levels were significantly associated with increased mortality. However, older obese or overweight individuals may have a decreased mortality risk. Thus, the findings of the current meta-analysis raise questions about the utility of the definition of metabolic syndrome in predicting all-cause mortality and CVD mortality in the elderly population.

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PMCID: PMC5690732
PMID: 29137039

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Cardiovascular Risk Burden and Future Risk of Walking Speed Limitation in Older Adults.

Heiland EG, Qiu C, Wang R, Santoni G, Liang Y, Fratiglioni L, Welmer AK.

OBJECTIVES: To explore the association between cardiovascular risk factor (CRF) burden and limitation in walking speed, balance, and chair stand and to verify whether these associations vary according to age and cognitive status.
DESIGN: Longitudinal population-based study.
SETTING: Urban area of Stockholm, Sweden.
PARTICIPANTS: Individuals aged 60 and older who participated in the Swedish National Study on Aging and Care in Kungsholmen and were free of limitations in walking speed (n = 1,441), balance (n = 1,154), or chair stands (n = 1,496) at baseline (2001-04).
MEASUREMENTS: At baseline, data on demographic characteristics, CRFs, other lifestyle factors, C-reactive protein, and cognitive function were collected. CRF burden was measured using the Framingham general cardiovascular risk score (FRS). Limitations in walking speed (<0.8 m/s), balance (<5 seconds), and chair stand (inability to rise 5 times) were determined at 3-, 6-, and 9-year follow-up. Data were analyzed using Cox proportional hazards models stratified according to age (<78, ≥78).
RESULTS: During follow-up, 326 persons developed limitations in walking speed, 303 in balance, and 374 in chair stands. An association between the FRS and walking speed limitation was evident only in adults younger than 78 (for each 1-point increase in FRS: hazard ratio (HR) = 1.09, 95% confidence interval (CI) = 1.02-1.17) after controlling for potential confounders including cognitive function (correspondingly, in adults aged ≥78: HR = 0.98, 95% CI = 0.92-1.03). Also, higher FRS was significantly associated with faster decline in walking speed (P < .001).
CONCLUSION: A higher FRS is associated with greater risk of subsequent development of walking speed limitation in adults younger than 78, independent of cognitive function. Interventions targeting multiple CRFs in younger-old people may help in maintaining mobility function.

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Sleep Apnea and Cardiovascular Disease: Lessons From Recent Trials and Need for Team Science.

Drager LF, McEvoy RD, Barbe F, Lorenzi-Filho G, Redline S; INCOSACT Initiative (International Collaboration of Sleep Apnea Cardiovascular Trialists).

Emerging research highlights the complex interrelationships between sleep-disordered breathing and cardiovascular disease, presenting clinical and research opportunities as well as challenges. Patients presenting to cardiology clinics have a high prevalence of obstructive and central sleep apnea associated with Cheyne-Stokes respiration. Multiple mechanisms have been identified by which sleep disturbances adversely affect cardiovascular structure and function. Epidemiological research indicates that obstructive sleep apnea is associated with increases in the incidence and progression of coronary heart disease, heart failure, stroke, and atrial fibrillation. Central sleep apnea associated with Cheyne-Stokes respiration predicts incident heart failure and atrial fibrillation; among patients with heart failure, it strongly predicts mortality. Thus, a strong literature provides the mechanistic and empirical bases for considering obstructive sleep apnea and central sleep apnea associated with Cheyne-Stokes respiration as potentially modifiable risk factors for cardiovascular disease. Data from small trials provide evidence that treatment of obstructive sleep apnea with continuous positive airway pressure improves not only patient-reported outcomes such as sleepiness, quality of life, and mood but also intermediate cardiovascular end points such as blood pressure, cardiac ejection fraction, vascular parameters, and arrhythmias. However, data from large-scale randomized controlled trials do not currently support a role for positive pressure therapies for reducing cardiovascular mortality. The results of 2 recent large randomized controlled trials, published in 2015 and 2016, raise questions about the effectiveness of pressure therapies in reducing clinical end points, although 1 trial supported the beneficial effect of continuous positive airway pressure on quality of life, mood, and work absenteeism. This review provides a contextual framework for interpreting the results of recent studies, key clinical messages, and suggestions for future sleep and cardiovascular research, which include further consideration of individual risk factors, use of existing and new multimodality therapies that also address adherence, and implementation of trials that are sufficiently powered to target end points and to support subgroup analyses. These goals may best be addressed through strengthening collaboration among the cardiology, sleep medicine, and clinical trial communities.

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PMID: 29109195

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Impact of Hypothyroidism on Occurrence and Outcome of Acute Coronary Syndrome from the National Inpatient Sample.

Dhital R, Basnet S, Poudel DR.

Thyroid hormones have a profound effect on cardiovascular physiology. We utilized a large national inpatient database in the United States (National Inpatient Sample) to study hypothyroidism in relation to the prevalence of coronary heart disease (CHD) and its impact on outcomes (mortality, the length of stay, and hospitalization cost) in the acute coronary syndrome (ACS) subgroup of CHD patients. We found that although hypothyroidism has an increased association with CHD (odds ratio [OR] 1.11, 95% confidence interval [CI] 1.09 to 1.12, $p<0.001$), the odds of developing ACS in these CHD patients is lower in the hypothyroid group (OR 0.71, 95% CI 0.70 to 0.72, $p<0.001$) after adjusting for multiple risk factors. Additionally, patients with hypothyroid ACS have a reduced odds of in-hospital mortality (OR 0.86, 95% CI 0.83 to 0.88, $p<0.001$), shorter length of stay by 0.45 days ($p<0.001$), and lower hospitalization cost by $1,531.45 ($p<0.001$) compared with the euthyroid group. Our findings suggest that hypothyroidism has an increased CHD risk but a lower risk of development of ACS in hospitalized CHD patients, as well as a better short-term prognosis including ACS-associated mortality.

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PMID: 29102035

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Midlife Systemic Inflammation, Late-Life White Matter Integrity, and Cerebral Small Vessel Disease: The Atherosclerosis Risk in Communities Study.

Walker KA, Power MC, Hoogeveen RC, Folsom AR, Ballantyne CM, Knopman DS, Windham BG, Selvin E, Jack CR Jr, Gottesman RF.

BACKGROUND AND PURPOSE: It is currently unclear whether midlife systemic inflammation promotes the development of white matter (WM) abnormalities and small vessel disease in the elderly. We examined the association of midlife systemic inflammation with late-life WM hyperintensity volume, deep and periventricular WM microstructural integrity (fractional anisotropy and mean diffusivity [MD]), cerebral infarcts, and microbleeds in a biracial prospective cohort study.
METHODS: Linear and logistic regression examined the relation between midlife high-sensitivity C-reactive protein (CRP)-a nonspecific marker of inflammation-and brain magnetic resonance imaging markers assessed 21 years later in the Atherosclerosis Risk in Communities Study.
RESULTS: We included 1485 participants (baseline age, 56[5]; 28% black). After adjusting for demographic factors and cardiovascular disease, each SD increase in midlife CRP was associated with lower fractional anisotropy (-0.09 SD; 95% confidence interval, -0.15 to -0.02) and greater MD (0.08 SD; 95% confidence interval, 0.03-0.15) in deep WM and lower fractional anisotropy (-0.07 SD; 95% confidence interval, -0.13 to 0.00) in periventricular WM. We found stronger associations between CRP and periventricular WM microstructural integrity among black participants (P interaction=0.011). Although an association between higher CRP levels and greater WM hyperintensity volume was found only among APOE ε4-positive participants in our primary analysis (0.14 SD; 95% confidence interval, 0.01-0.26; P interaction=0.028), this relationship extended to the entire sample after accounting for differential attrition. Midlife CRP was not associated with the presence of cerebral infarcts or microbleeds in late life.
CONCLUSIONS: Our findings support the hypothesis that midlife systemic inflammation may promote the development of chronic microangiopathic structural WM abnormalities in the elderly.

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PMCID: PMC5705320 [Available on 2018-12-01]
PMID: 29101255

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Subclinical Atherosclerosis Among Young and Middle-Aged Adults Using Carotid Intima-Media Thickness Measurements.

Jones DL, Rodriguez VJ, Alcaide ML, Barylski N, Cabral D, Rundek T, Weiss SM, Kumar M.

OBJECTIVES: The presence of atherosclerotic plaque in the carotid arteries is a strong predictor of cardiovascular disease (CVD). Research and data on CVD risk have been derived primarily from individuals aged 55 years or older, and assessment of CVD risk among young and middle-aged adults seldom has been studied. The use of ultrasonography to measure carotid intima-media thickness (IMT) and carotid plaque appears to have utility to detect subclinical atherosclerosis in asymptomatic adults. This study evaluated the presence of carotid plaque using ultrasonography among healthy young and middle-aged adults.

METHODS: Participants were men and women recruited in Miami, Florida, and were 18 to 50 years old with no history of CVD. Participants underwent a general physical examination and carotid artery ultrasonography to evaluate carotid IMT and carotid plaque.

RESULTS: From a total of 173 participants with a mean age of 34 years (standard deviation 8.9), 21.0% (95% confidence interval [CI] 15.0-27.2) were identified as having carotid plaque. IMT values ranged from 0.49 to 1.03 mm, with a mean value of 0.70 mm (standard deviation 0.09). In multivariable logistic regression older age (adjusted odds ratio [AOR] 1.08, 95% CI 1.01-1.16, P = 0.024) and cigarette smoking (AOR 2.67, 95% CI 1.02-7.00, P = 0.045) were associated with plaque, after controlling for IMT (AOR 2.55, 95% CI 1.40-4.65, P = 0.002).

CONCLUSIONS: Traditional CVD risk factors such as those evaluated in this study may fail to provide adequate predictive value of carotid atherosclerosis in younger populations with no history of CVD, because the majority of traditional risk factors identified in previous research were not associated with carotid plaque in this young sample. Further research assessing nontraditional risk factors among asymptomatic individuals is required, and the evaluation of IMT as an intervention tool to detect CVD risk in these asymptomatic populations is warranted.

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PMID: 29100226

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Stress-Induced Cardiomyopathy in Cancer Patients.

Giza DE, Lopez-Mattei J, Vejpongsa P, Munoz E, Iliescu G,Kitkungvan D, Hassan SA, Kim P, Ewer MS, Iliescu C.

Takotsubo syndrome, also known as stress-induced cardiomyopathy (SC), is underrecognized in cancer patients. This study aims to investigate the incidence, natural history, and triggers of SC in cancer patients and its impact on cancer therapy and overall survival. A total of 30 subjects fulfilled the diagnostic criteria for SC at MD Anderson Cancer Center over a 6-year period. Clinical presentation, electrocardiogram, laboratory data, and transthoracic echocardiogram results registered during the acute phase and follow-up were collected. All patients underwent coronary angiography. The most frequent presenting symptoms were chest pain in 63.3% of the patients and shortness of breath/dyspnea on exertion in 27% of the patients. T-wave inversion was a more common electrocardiographic presentation (60%) than ST elevation (13.3%). The median and interquartile range of peak creatine kinase MB fraction, troponin I, and brain natriuretic peptide were creatine kinase MB fraction 8.9, 4.6 to 21.1; troponin I 1.31, 0.7 to 3.3; and brain natriuretic peptide 1,124, 453.5 to 2,369.5. The most common complication of SC was cardiogenic shock requiring inotropic agents (20%). Of the 21 patients who required ongoing cancer treatment, 16 were able to resume chemotherapy, 5 underwent surgery, and 4 received radiation treatment. Median time to resume cancer treatment was 20 days after SC. None of the patients experienced recurrence of SC and other cardiac events. In conclusion, SC should be considered in the differential diagnosis of cancer patients who present with chest pain and ECG findings characteristic of acute coronary syndrome. Most of these patients normalize ejection fraction and may resume cancer therapy early.

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PMID: 29096885

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The association between tinnitus and the risk of ischemic cerebrovascular disease in young and middle-aged patients: A secondary case-control analysis of a nationwide, population-based health claims database.

Huang YS, Koo M, Chen JC, Hwang JH.

BACKGROUND: Tinnitus and ischemic cerebrovascular disease (ICVD) may share common pathophysiologic mechanisms. Nevertheless, no studies have investigated whether tinnitus is associated with a higher risk of ICVD. The aim of this study was to evaluate the risk of ICVD among young and middle-aged patients with tinnitus.
METHODS: Using the Taiwan's National Health Insurance Research Database, we identified 3,474 patients 20-45 years old with incident ICVD diagnosed between January 1, 2000 and December 31, 2010 and 17,370 controls, frequency matched on age interval, sex, and year of the index date. Risk of ICVD associated with tinnitus was assessed using multiple logistic regression analyses.
RESULTS: Tinnitus was significantly associated with a higher risk of incident ICVD among young and middle-aged patients (adjusted odds ratio [OR] 1.66, 95% confidence interval [CI] 1.34-2.04), adjusting for sex, age, and comorbidities. In addition, sex-stratified analysis showed that the associations were significant in both male (adjusted OR 1.55, 95% CI 1.16-2.07) and female patients (adjusted OR 1.77, 95% CI 1.30-2.41). Furthermore, tinnitus was significantly associated with a higher risk of ICVD in the 20.0-29.9 years (adjusted OR 4.11, 95% CI 1.98-8.52) and 30.0-39.9 years (adjusted OR 2.19, 95% CI 1.57-3.05) age groups, but not in the 40.0-45.0 years age group.
CONCLUSIONS: Tinnitus could be a novel risk factor or clinical indicator for young ischemic stroke, and further investigations are warranted.

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PMID: 29095920

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Fatness and Fitness With Cardiometabolic Risk Factors in Adolescents.

Demmer DL, Beilin LJ, Hands B, Burrows S, Cox KL, Oddy WH, Mori TA.

Context: The relative importance of fitness and fatness with cardiometabolic risk factors is uncertain during the crucial developmental stage of late adolescence.
Objective: We aimed to compare the concurrent influences of cardiorespiratory fitness and fatness in relationship to cardiometabolic risk factors in adolescents from the Western Australian Pregnancy Cohort Study.
Design, Setting, and Participants: Cross-sectional analysis was performed on 1128 participants with complete blood pressure (BP) data and 963 participants with complete blood biochemistry at 17 years of age. Fatness (waist circumference) and cardiorespiratory fitness (physical work capacity 170) were assessed as continuous measures to avoid the use of arbitrary cut points. Analyses used linear regression models adjusted for sex and potential lifestyle confounders.
Main Outcome Measure: Cardiometabolic risk factors.
Results: Fatness was positively associated with systolic BP (coefficient, 0.19; $P < 0.001$; β coefficient, 0.20), triglycerides (log coefficient, 0.009; $P < 0.001$; β coefficient, 0.24), low-density lipoprotein cholesterol (coefficient, 0.005; $P = 0.007$; β coefficient, 0.10), and high-sensitivity C-reactive protein (log coefficient, 0.05; $P < 0.001$; β coefficient, 0.35). There were no significant effects of fitness on any of these measures. A positive association between homeostasis model of assessment for insulin resistance and fatness (log coefficient, 0.02; $P < 0.001$; β coefficient, 0.33) was attenuated by fitness (log coefficient, -0.0.18; $P < 0.001$; β coefficient, -0.18). Fatness was inversely associated with high-density lipoprotein cholesterol (HDL-C) in both sexes (coefficient, -0.006; $P < 0.001$; β coefficient, -0.23), whereas fitness was positively associated with HDL-C only in females (coefficient, 0.08; $P = 0.03$; β coefficient, 0.15).
Conclusions: The adverse effects of central adiposity seen across a broad range of cardiometabolic risk factors were only partially ameliorated by fitness in this adolescent population.

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PMID: 29088412

Hypertension. 2018 Jan;71(1):168-176.

Relationships Between Components of Blood Pressure and Cardiovascular Events in Patients with Stable Coronary Artery Disease and Hypertension.

Vidal-Petiot E, Greenlaw N, Ford I, Ferrari R, Fox KM, Tardif JC, Tendera M, Parkhomenko A, Bhatt DL, Steg PG.

Observational studies have shown a J-shaped relationship between diastolic blood pressure (BP) and cardiovascular events in hypertensive patients with coronary artery disease. We investigated whether the increased risk associated with low diastolic BP reflects elevated pulse pressure (PP). In 22672 hypertensive patients with coronary artery disease from the CLARIFY registry (Prospective Observational Longitudinal Registry of Patients With Stable Coronary Artery Disease), followed for a median of 5.0 years, BP was measured annually and averaged. The relationships between PP and diastolic BP, alone or combined, and the primary composite outcome (cardiovascular death or myocardial infarction) were analyzed using multivariable Cox proportional hazards models. Adjusted hazard ratios for the primary outcome were 1.62 (95% confidence interval [CI], 1.40-1.87), 1.00 (ref), 1.07 (95% CI, 0.94-1.21), 1.54 (95% CI, 1.32-1.79), and 2.34 (95% CI, 1.95-2.81) for PP<45, 45 to 54 (reference), 55 to 64, 65 to 74, and ≥75 mm Hg, respectively, and 1.50 (95% CI, 1.31-1.72), 1.00 (reference), and 1.58 (95% CI, 1.42-1.77) for diastolic BPs of <70, 70 to 79 (ref), and ≥80 mm Hg, respectively. In a cross-classification analysis between diastolic BP and PP, the relationship between diastolic BP and the primary outcome remained J-shaped when the analysis was restricted to patients with the lowest-risk PP (45-64 mm Hg), with adjusted hazard ratios of 1.53 (95% CI, 1.27-1.83), 1.00 (ref), and 1.54 (95% CI, 1.34-1.75) in the <70, 70 to 79 (reference), and ≥80 mm Hg subgroups, respectively. The J-shaped relationship between diastolic BP and cardiovascular events in hypertensive patients with coronary artery disease persists in patients within the lowest-risk PP range and is therefore unlikely to be solely the consequence of an increased PP reflecting advanced vascular disease. CLINICAL TRIAL REGISTRATION: URL: http://www.clarify-registry.com. Unique identifier: ISRCTN43070564.

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PMID: 29084876

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Relationship between Mediterranean diet and asymptomatic peripheral arterial disease in a population of pre-menopausal women.

Mattioli AV, Coppi F, Migaldi M, Scicchitano P, Ciccone MM, Farinetti A.

BACKGROUND AND AIMS: The Mediterranean Diet (MedD) is considered a very healthy diet useful in the prevention of cardiovascular disease. The present study aims to evaluate adherence to MedD in unselected premenopausal women and its relation with ankle-brachial index (ABI), an index of preclinical atherosclerosis.

METHODS AND RESULTS: A group of 425 patients (age range 45-54 years) was investigated. They were enrolled only if they were asymptomatic for cardiovascular disease. Nutritional parameters were assessed by a self-administered food frequency validated questionnaire (116 items) completed by an interviewer administered 24 h diet recall. They all underwent ABI measurement. The mean MedD Score was 32.2 ± 6.1 (Q1-Q3 range 26-37) comparing with data from Italian population (46 ± 8.3) was significantly lower. Intake of food categories sources of antioxidants was higher in patients with a greater adherence to Med D and was mainly related to fruit and vegetables. Patients were categorized in quartile according to MedD Score and we evaluate the distribution of ABI index within quartile. 31.4% of women in Q1 (lower adherence to MedD) had an ABI lower than 0.9 compared to 18.3% of women in Q4 (higher adherence to MedD): $p < 0.01$.Obesity was more frequent in Q1 compared to Q4 and in women with lower ABI.

CONCLUSIONS: Women with a low MedD Score were more obese and showed instrumental sign of preclinical peripheral atherosclerosis. MedD rich in antioxidants from fruit, vegetables and nuts influenced the development of atherosclerosis and was associated with a lower incidence of asymptomatic atherosclerosis.

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Prevalence, risk factors, and prognostic significance of masked hypertension in diabetic patients.

Zhao H, Zeng F, Wang X, Wang L.

The aims of present study were to evaluate the prevalence, risk factors, and prognostic significance of masked hypertension in diabetic patients. Using a cross-sectional design, 266 patients with documented type 2 diabetes mellitus and clinic blood pressure (BP) <140/90mm Hg without antihypertension treatment were enrolled; 24-hour ambulatory BP monitoring was applied to evaluate mean 24-hour systolic/diastolic BP. Demographics, medical histories, and medications usage were obtained using questionnaire. Fasting venous blood was drawn for biochemical analysis. Approximately 26.5% of participants were diagnosed as masked hypertension with mean 24-hour systolic BP >130mm Hg and/or mean 24-hour diastolic BP >80mm Hg. Compared with those without masked hypertension, other than significantly higher mean 24-hour systolic/diastolic BP, patients with masked hypertension were more elderly, had higher serum glycated hemoglobin (HbA1c) and C-reactive protein (CRP) levels and higher prevalence of coronary heart disease (CHD). Multivariate regression analysis showed that aging, increased HbA1c and CRP levels, and prevalent CHD were independently associated with masked hypertension. Logistic regression analysis revealed that after adjusted for traditional risk factors including age, male sex, smoking status, low-density lipoprotein-cholesterol, CRP, clinic systolic BP, and HbA1c, masked hypertension remained independently associated with prevalent cardiovascular disease (CVD), with odds ratio of 1.31 and 95% confidence interval of 1.11 to 1.85. In summary, in diabetic patients, concurrent masked hypertension increases the odds of having CVD. Future randomized controlled trials are warranted to investigate whether screening and managing masked hypertension could reduce cardiovascular events in diabetic patients.

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PMID: 29069022

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Individual testosterone decline and future mortality risk in men.

Holmboe SA, Skakkebæk NE, Juul A, Scheike T, Jensen TK, Linneberg A, Thuesen BH, Andersson AM.

OBJECTIVE: Male aging is characterized by a decline in testosterone (TS) levels with a substantial variability between subjects. However, it is unclear whether differences in age-related changes in TS are associated with general health. We investigated associations between mortality and intra-individual changes in serum levels of total TS, SHBG, free TS and LH during a ten-year period with up to 18 years of registry follow-up.
DESIGN: 1167 men aged 30-60 years participating in the Danish Monitoring Trends and Determinants of Cardiovascular Disease (MONICA1) study and who had a follow-up examination ten years later (MONICA10) were included. From MONICA10, the men were followed up to 18 years (mean: 15.2 years) based on the information from national mortality registries via their unique personal ID numbers.
METHODS: Cox proportional hazard models were used to investigate the association between intra-individual hormone changes and all-cause, CVD and cancer mortalities.
RESULTS: A total of 421 men (36.1%) died during the follow-up period. Men with most pronounced decline in total TS (<10th percentile) had a higher all-cause mortality risk compared to men within the 10th to 90th percentile (hazard ratio (HR): 1.60; 95% confidence interval (CI): 1.08-2.36). No consistent associations were seen in cause-specific mortality analyses.
CONCLUSION: Our study showed that higher mortality rates were seen among the men who had the most pronounced age-related decline in TS, independent of their baseline TS levels.

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PMID: 29066571

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Association of central blood pressure and cardiovascular diseases in diabetic patients with hypertension.

Yang L, Qin B, Zhang X, Chen Y, Hou J.

To evaluate association of central blood pressure (BP) and cardiovascular disease (CVD) in diabetic patients with hypertension. This was a cross-section study and 360 participants were enrolled. Baseline characteristics were collected and indices of central BP including central systolic/diastolic BP (SBP/DBP), augmentation index adjusted for 75 beats per minute of heart rate (AIx@75) were measured. Participants were separated into with and without CVD groups and between-group differences were assessed. Linear regression analysis was used to evaluate potential risk factors for increased AIx@75. Logistic regression analysis was used to evaluate association between central SBP and AIx@75 with CVD.Mean age was 50.6 years and male participants accounted for 57.8%. Thirty-five and 43 participants had coronary heart disease and ischemic stroke. Compared with participants without CVD, those with CVD were more likely to be male and smokers and had higher glycated hemoglobin level. Additionally, participants with CVD had significantly higher central SBP and AIx@75 compared with those without CVD. Ageing, male gender, and presence of coronary heart disease and ischemic stroke were associated with increased AIx@75, whereas renin-angiotensin-axis inhibitor was associated with reduced AIx@75. After adjusted for traditional risk factors including brachial SBP, both central SBP, and AIx@75 remained significantly associated with CVD, with odds ratio and 95% confidence interval of 1.09 (1.08-1.31) and 1.20 (1.15-1.42), respectively. Diabetic patients with hypertension, ageing, male gender, and presence of CVD are independent risk factors of central BP increase; and increased central SBP and AIx@75 are significantly associated with CVD.

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PMID: 29049227

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Lipid profile, cardiovascular disease and mortality in a Mediterranean high-risk population: The ESCARVAL-RISK study.

Orozco-Beltran D, Gil-Guillen VF, Redon J, Martin-Moreno JM, Pallares-Carratala V, Navarro-Perez J, Valls-Roca F, Sanchis-Domenech C, Fernandez-Gimenez A, Perez-Navarro A, Bertomeu-Martinez V, Bertomeu-Gonzalez V, Cordero A, Pascual de la Torre M, Trillo JL, Carratala-Munuera C, Pita-Fernandez S, Uso R, Durazo-Arvizu R, Cooper R, Sanz G, Castellano JM, Ascaso JF, Carmena R, Tellez-Plaza M; ESCARVAL Study Group.

INTRODUCTION: The potential impact of targeting different components of an adverse lipid profile in populations with multiple cardiovascular risk factors is not completely clear. This study aims to assess the association between different components of the standard lipid profile with all-cause mortality and hospitalization due to cardiovascular events in a high-risk population.

METHODS: This prospective registry included high risk adults over 30 years old free of cardiovascular disease (2008-2012). Diagnosis of hypertension, dyslipidemia or diabetes mellitus was inclusion criterion. Lipid biomarkers were evaluated. Primary endpoints were all-cause mortality and hospital admission due to coronary heart disease or stroke. We estimated adjusted rate ratios (aRR), absolute risk differences and population attributable risk associated with adverse lipid profiles.

RESULTS: 51,462 subjects were included with a mean age of 62.6 years (47.6% men). During an average follow-up of 3.2 years, 919 deaths, 1666 hospitalizations for coronary heart disease and 1510 hospitalizations for stroke were recorded. The parameters that showed an increased rate for total mortality, coronary heart disease and stroke hospitalization were, respectively, low HDL-Cholesterol: aRR 1.25, 1.29 and 1.23; high Total/HDL-Cholesterol: aRR 1.22, 1.38 and 1.25; and high Triglycerides/HDL-Cholesterol: aRR 1.21, 1.30, 1.09. The parameters that showed highest population attributable risk (%) were, respectively, low HDL-Cholesterol: 7.70, 11.42, 8.40; high Total/HDL-Cholesterol: 6.55, 12.47, 8.73; and high Triglycerides/HDL-Cholesterol: 8.94, 15.09, 6.92.

CONCLUSIONS: In a population with cardiovascular risk factors, HDL-cholesterol, Total/HDL-cholesterol and triglycerides/HDL-cholesterol ratios were associated with a higher population attributable risk for cardiovascular disease compared to other common biomarkers.

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PMID: 29045483

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The association between serum brain-derived neurotrophic factor and a cluster of cardiovascular risk factors in adolescents: The CHAMPS-study DK.

Pedersen NH, Tarp J, Andersen LB, Gejl AK, Huang T, Peijs L, Bugge A.

BACKGROUND AND OBJECTIVE: Cardiovascular disease and type 2 diabetes pose a global health burden. Therefore, clarifying the pathology of these risk factors is essential. Previous studies have found positive and negative associations between one or more cardiovascular risk factors and brain-derived neurotrophic factor (BDNF) probably due to diverse methodological approaches when analyzing peripheral BDNF levels. Moreover, only a few studies have been performed in youth populations. Consequently, the main objective of this study was to examine the association between serum BDNF and a composite z-score consisting of six cardiovascular risk factors. A secondary aim was to examine the associations between serum BDNF and each of the six risk factors.

METHODS: Four hundred and forty-seven apparently healthy adolescents between 11-17 years of age participated in this cross-sectional study. Cardiorespiratory fitness (CRF), anthropometrics, pubertal status, blood pressure (BP), serum BDNF, high-density lipoprotein cholesterol (HDL-C), triglyceride (TG), blood glucose and insulin were measured. Information about alcohol consumption and socio-economic status was collected via questionnaires. Associations were modelled using linear regression analysis.

RESULTS: Serum BDNF was positively associated with the composite z-score in the total study sample (standardized beta coefficient (std.β) = 0.10, P = 0.037). In males, serum BDNF was positively associated with the composite z-score (Std. β = 0.14, P = 0.034) and HOMA-IR (Std. β = 0.19, P = 0.004), and negatively associated with CRF (Std. β = -0.15, P = 0.026). In females, BDNF was positively associated with TG (Std. β = 0.14, P = 0.030) and negatively associated with waist circumference (WC) (Std. β = -0.16, P = 0.012).

CONCLUSION: Serum BDNF was positively associated with a composite z-score of cardiovascular risk factors. This association seems to be mainly driven by the association between TG, HOMA-IR and serum BDNF, and particularly for males. Further longitudinal research is warranted to determine the temporal relationship between BDNF and cardiovascular risk factors.

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PMID: 29028824

Neurology. 2017 Nov 7;89(19):1985-1994.

Increasing prevalence of vascular risk factors in patients with stroke: A call to action.

Otite FO, Liaw N, Khandelwal P, Malik AM, Romano JG, Rundek T, Sacco RL, Chaturvedi S.

OBJECTIVE: To evaluate trends in prevalence of cardiovascular risk factors (hypertension, diabetes, dyslipidemia, smoking, and drug abuse) and cardiovascular diseases (carotid stenosis, chronic renal failure [CRF], and coronary artery disease [CAD]) in acute ischemic stroke (AIS) in the United States.

METHODS: We used the 2004-2014 National Inpatient Sample to compute weighted prevalence of each risk factor in hospitalized patients with AIS and used joinpoint regression to evaluate change in prevalence over time.

RESULTS: Across the 2004-2014 period, 92.5% of patients with AIS had ≥1 risk factor. Overall age- and sex-adjusted prevalence of hypertension, diabetes, dyslipidemia, smoking, and drug abuse were 79%, 34%, 47%, 15%, and 2%, respectively, while those of carotid stenosis, CRF, and CAD were 13%, 12%, and 27%, respectively. Risk factor prevalence varied by age (hypertension: 44% in 18-39 years vs 82% in 60-79 years), race (diabetes: Hispanic 49% vs white 30%), and sex (drug abuse: men 3% vs women 1.4%). Using joinpoint regression, prevalence of hypertension increased annually by 1.4%, diabetes by 2%, dyslipidemia by 7%, smoking by 5%, and drug abuse by 7%. Prevalence of CRF, carotid stenosis, and CAD increased annually by 13%, 6%, and 1%, respectively. Proportion of patients with multiple risk factors also increased over time.

CONCLUSIONS: Despite numerous guidelines and prevention initiatives, prevalence of hypertension, diabetes, dyslipidemia, smoking, and drug abuse in AIS increased across the 2004-2014 period. Proportion of patients with carotid stenosis, CRF, and multiple risk factors also increased. Enhanced risk factor modification strategies and implementation of evidence-based recommendations are needed for optimal stroke prevention.

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PMID: 29021359

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Cardiovascular disease risk and androgen deprivation therapy in patients with localised prostate cancer: a prospective cohort study.

Haque R, UlcickasYood M, Xu X, Cassidy-Bushrow AE, Tsai HT, Keating NL, Van Den Eeden SK, Potosky AL.

BACKGROUND: As androgen deprivation therapy (ADT) is increasingly being used in men with localised prostate cancer, our goal was to examine the association between ADT and the risk of cardiovascular disease (CVD).
METHODS: We conducted a prospective cohort study using records of a large health-care system in California. The study included men with newly diagnosed localised prostate cancer (1998-2008) who initially underwent active surveillance (N=7637) and were followed through 2010. We examined 10 individual CVD outcomes. Cox proportional hazard models incorporated time-varying treatment variables and controlled for race/ethnicity, age, and tumour characteristics, recurrence risk, CVD medication use, and CVD risk factors.
RESULTS: Of the 7637 subjects, nearly 30% were exposed to ADT. In the multivariable analyses, ADT was associated with an increased risk of heart failure (adjusted HR=1.81, 95% CI 1.40-2.32) in men without preexisting CVD. Elevated risks of arrhythmia (adjusted HR=1.44, 95% CI 1.02-2.01), and conduction disorder (adjusted HR=3.11, 95% CI 1.22, 7.91) were only observed among patients with preexisting CVD.
CONCLUSIONS: In men with clinically localised prostate cancer who were initially under active surveillance, ADT was associated with a greater risk of heart failure in men without any preexisting CVD. We also found an increased risk of arrhythmia and conduction disorder in men with preexisting CVD. This study provides the basis for identifying high-risk men treated with ADT who might benefit from regular cardiac monitoring and lifestyle modification recommendations.

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PMCID: PMC5674100 [Available on 2018-10-10]
PMID: 29017178

J Am Coll Cardiol. 2017 Oct 10;70(15):1833-1842.

The Importance of Breakfast in Atherosclerosis Disease: Insights From the PESA Study.

Uzhova I, Fuster V, Fernández-Ortiz A, Ordovás JM, Sanz J, Fernández-Friera L, López-Melgar B, Mendiguren JM, Ibáñez B, Bueno H, Peñalvo JL.

BACKGROUND: Daily habits, including the number and quality of eating occasions, are potential targets for primary prevention strategies with large health impacts. Skipping breakfast is considered a frequent and unhealthy habit associated with an increased cardiovascular (CV) risk.
OBJECTIVES: The study sought to explore the association between different breakfast patterns and CV risk factors and the presence, distribution, and extension of subclinical atherosclerosis.
METHODS: Cross-sectional analysis was performed within the PESA (Progression of Early Subclinical Atherosclerosis) study, a prospective cohort of asymptomatic (free of CV events at baseline) adults 40 to 54 years of age. Lifestyle and multivascular imaging data along with clinical covariates were collected from 4,052 participants. Multivariate logistic regression models were used in the analysis.
RESULTS: Three patterns of breakfast consumption were studied: high-energy breakfast, when contributing to >20% of total daily energy intake (27% of the population); low-energy breakfast, when contributing between 5% and 20% of total daily energy intake (70% of the population); and skipping breakfast, when consuming <5% of total daily energy (3% of the population). Independent of the presence of traditional and dietary CV risk factors, and compared with high-energy breakfast, habitual skipping breakfast was associated with a higher prevalence of noncoronary (odds ratio: 1.55; 95% confidence interval: 0.97 to 2.46) and generalized (odds ratio: 2.57; 95% confidence interval: 1.54 to 4.31) atherosclerosis.
CONCLUSION: Skipping breakfast is associated with an increased odds of prevalent noncoronary and generalized atherosclerosis independently of the presence of conventional CV risk factors. (Progression of Early Subclinical Atherosclerosis [PESA]; NCT01410318).

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PMID: 28982495

N Z Med J. 2017 Oct 6;130(1463):28-38.

An observational study of how clinicians use cardiovascular risk assessment to inform statin prescribing decisions.

Robinson T, Jackson R, Wells S, Kerr A, Marshall R.

AIM: Cardiovascular disease (CVD) risk assessment is commonly recommended in guidelines, but there is uncertainty about how clinicians use this information. Our objective was to understand how New Zealand primary care clinicians use CVD risk assessment estimates to inform new statin prescribing.

METHODS: We used a cohort of patients seen in primary care who have had a CVD risk estimated on the basis of a New Zealand modified Framingham risk equation. These patients were linked to national pharmaceutical dispensing records to determine new statin use in the following six months. Regression discontinuity and logistic regression analysis, and graphical approaches, were used to explore associations between estimated CVD risk and primary clinicians' decisions to initiate statin treatment.

RESULTS: There were 76,571 patients aged 35 to 75 who were not on a statin, had a first recorded CVD risk assessment between July 2007 and June 2011, and for whom national guidelines recommended management on the basis of estimated CVD risk. Statin dispensing increased with increasing CVD risk. There was no evidence of sudden jumps in the proportions of patients dispensed statins at guideline recommended treatment threshold values of 15% and 20% CVD risk (P=0.314 and 0.731). A logistic regression model using the CVD risk score predicted statin initiation better than models using lipid measures (Area Under the Curve 0.725 versus 0.682). However, further modelling and graphical analysis suggested clinicians were using a range of other information to inform the initiation of statins.

CONCLUSION: New Zealand primary care clinicians' statin prescribing decisions appear to be influenced by patients' predicted CVD risk. However, other factors are associated with increased statin dispensing independent of CVD risk score.

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Association of Glycemic Control With Reduced Risk for Large-Vessel Disease After More Than 50 Years of Type 1 Diabetes.

Tinsley LJ, Kupelian V, D'Eon SA, Pober D, Sun JK, King GL, Keenan HA.

Context: Previously we demonstrated, in individuals who have had type 1 diabetes (T1D) for 50 or more years (Medalists), that glycemic control was unrelated to diabetic complications, with the exception of cardiovascular disease (CVD), contrary to what has been documented in registry-based studies.
Objective: The purpose of this study is to validate these initial findings and identify contributors to mortality on an individual basis in a large cohort.
Design: Cross-sectional and longitudinal study.
Setting: Joslin Diabetes Center (JDC), Boston, Massachusetts.
Patients: 50-year Medalists presenting to JDC for study participation.
Interventions: None.
Main Outcomes Measures: Microvascular and macrovascular complications of diabetes and mortality.
Results: Glycemic control was not significantly associated with small-vessel complications in Medalists but was associated with CVD in the overall cohort, yet with varying effect by tertile of cohort duration. CVD was the largest contributor to mortality, whereas hemoglobin A1c was not an independent predictor of mortality either overall or substantially by diagnosis interval. Additionally, exercise mitigated mortality risk imparted by CVD.
Conclusions: Few large populations with long duration of (T1D) have been available to examine the effects of long-term exposure to hyperglycemia. These data indicate that an association of glycemic control, complications, and mortality may change in an older population with T1D. These results suggest that careful control is still warranted in older populations with T1D.

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PMID: 28973526

Brain. 2017 Oct 1;140(10):2653-2662.

Migraine and risk of stroke: a national population-based twin study.

Lantz M, Sieurin J, Sjölander A, Waldenlind E, Sjöstrand C, Wirdefeldt K.

Numerous studies have indicated an increased risk for stroke in patients with migraine, especially migraine with aura; however, many studies used self-reported migraine and only a few controlled for familial factors. We aimed to investigate migraine as a risk factor for stroke in a Swedish population-based twin cohort, and whether familial factors contribute to an increased risk. The study population included twins without prior cerebrovascular disease who answered a headache questionnaire during 1998 and 2002 for twins born 1935-58 and during 2005-06 for twins born between 1959 and 1985. Migraine with and without aura and probable migraine was defined by an algorithm mapping on to clinical diagnostic criteria according to the International Classification of Headache Disorders. Stroke diagnoses were obtained from the national patient and cause of death registers. Twins were followed longitudinally, by linkage of national registers, from date of interview until date of first stroke, death, or end of study on 31 Dec 2014. In total, 8635 twins had any migraineous headache, whereof 3553 had migraine with aura and 5082 had non-aura migraineous headache (including migraine without aura and probable migraine), and 44 769 twins had no migraine. During a mean follow-up time of 11.9 years we observed 1297 incident cases of stroke. The Cox proportional hazards model with attained age as underlying time scale was used to estimate hazard ratios with 95% confidence intervals for stroke including ischaemic and haemorrhagic subtypes related to migraine with aura, non-aura migraineous headache, and any migraineous headache. Analyses were adjusted for gender and cardiovascular risk factors. Where appropriate; within-pair analyses were performed to control for confounding by familial factors. The age- and gender-adjusted hazard ratio for stroke related to migraine with aura was 1.27 (95% confidence interval 1.00-1.62), P = 0.05, and 1.07 (95% confidence interval 0.91-1.26), P = 0.39 related to any migraineous headache. Multivariable adjusted analyses showed similar results. When stratified by gender and attained age of ≤50 or >50 years, the estimated hazard ratio for stroke was higher in twins younger than 50 years and in females; however, non-significant. In the within-pair analysis, the hazard ratio for stroke related to migraine with aura was attenuated [hazard ratio 1.09 (95% confidence interval 0.81-1.46), P = 0.59].

In conclusion, we observed no increased stroke risk related to migraine overall but there was a modestly increased risk for stroke related to migraine with aura, and within-pair analyses suggested that familial factors might contribute to this association.

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PMID: 28969391

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Fish intake is associated with lower cardiovascular risk in a Mediterranean population: Prospective results from the Moli-sani study.

Bonaccio M, Ruggiero E, Di Castelnuovo A, Costanzo S, Persichillo M, De Curtis A, Cerletti C, Donati MB, de Gaetano G, Iacoviello L; Moli-sani study Investigators.

BACKGROUND AND AIMS: Fish consumption reportedly reduces the risk of heart disease, but the evidence of cardiovascular advantages associated with fish intake within Mediterranean cohorts is limited. The aim of this study was to test the association between fish intake and risk of composite coronary heart disease (CHD) and stroke in a large population-based cohort adhering to Mediterranean Diet.

METHODS AND RESULTS: Prospective analysis on 20,969 subjects free from cardiovascular disease at baseline, enrolled in the Moli-sani study (2005-2010). Food intake was recorded by the Italian version of the EPIC food frequency questionnaire. Hazard ratios were calculated by using multivariable Cox-proportional hazard models. During a median follow-up of 4.3 years, a total of 352 events occurred (n of CHD = 287 and n of stroke = 66). After adjustment for a large panel of covariates, fish intake ≥4 times per week was associated with 40% reduced risk of composite CHD and stroke (HR = 0.60; 95%CI 0.40-0.90), and with 40% lower risk of CHD (HR = 0.60; 95%CI 0.38-0.94) as compared with subjects in the lowest category of intake (<2 times/week). A similar trend of protection was found for stroke risk although results were not significant (HR = 0.62; 95%CI 0.26-1.51). When fish types were considered, protection against the composite outcome and CHD was confined to fatty fish intake.

CONCLUSIONS: Fish intake was associated with reduced risk of composite fatal and non-fatal CHD and stroke in a general Mediterranean population. The favourable association was likely to be driven by fatty fish.

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PMID: 28967596

Nutr Metab Cardiovasc Dis. 2017 Nov;27(11):939-948.

A systematic review on the relations between pasta consumption and cardio-metabolic risk factors.

Huang M, Li J, Ha MA, Riccardi G, Liu S.

AIMS: The traditional Italian dish pasta is a major food source of starch with low glycemic index (GI) and an important low-GI component of the Mediterranean diet. This systematic review aimed at assessing comprehensively and in-depth the potential benefit of pasta on cardio-metabolic disease risk factors.

DATA SYNTHESIS: Following a standard protocol, we conducted a systematic literature search of PubMed, CINAHL, and Cochrane Central Register of Controlled Trials for prospective cohort studies and randomized controlled dietary intervention trials that examined pasta and pasta-related fiber and grain intake in relation to cardio-metabolic risk factors of interest. Studies comparing postprandial glucose response to pasta with that to bread or potato were quantitatively summarized using meta-analysis of standardized mean difference. Evidence from studies with pasta as part of low-GI dietary intervention and studies investigating different types of pasta were qualitatively summarized.

CONCLUSIONS: Pasta meals have significantly lower postprandial glucose response than bread or potato meals, but evidence was lacking in terms of how the intake of pasta can influence cardio-metabolic disease risk. More long-term randomized controlled trials are needed where investigators directly contrast the cardio-metabolic effects of pasta and bread or potato. Long-term prospective cohort studies with required data available should also be analyzed regarding the effect of pasta intake on disease endpoints.

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PMID: 28954707

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Maternal Thyroid Antibodies Associates With Cardiometabolic Risk Factors in Children at the Age of 16.

Heikkinen AL, Päkkilä F, Hartikainen AL, Vääräsmäki M, Männistö T, Suvanto E.

Context and Objective: The objective of this study was to determine the effects of maternal thyroid dysfunction or antibodies during pregnancy on the cardiometabolic risk factors in children.
Design, Setting, and Participants: This prospective population-based cohort study, Northern Finland Birth Cohort 1986, included all pregnancies within a year in the area. Maternal serum samples were collected before the 20th week of gestation and analyzed for thyrotropin, free T4, thyroid-peroxidase antibodies (TPO-Abs), and thyroglobulin antibodies (Tg-Abs). Cardiometabolic risk factors in children at the age of 16 years were evaluated via blood sampling and clinical examination. Data were available for 3229 to 4176 mother-child pairs.
Main Outcome Measures: Waist circumference, blood pressure, lipids and lipoproteins, and insulin resistance were measured. Odds ratios (ORs) with 95% confidence intervals (CIs) of cardiometabolic risk factors in children with and without mothers with thyroid dysfunction or antibodies were calculated with logistic regression and adjusted for covariates. Results: Children of TPO-Ab-positive mothers had higher odds of metabolic syndrome (OR, 2.57; 95%, CI 1.26 to 5.25) and waist circumference indicative of metabolic syndrome (OR, 1.69; 95% CI, 1.14 to 2.50). They were also more likely to be overweight or obese (OR, 1.56; 95% CI, 1.04 to 2.34). Maternal thyroid dysfunction or Tg-Ab positivity did not associate with cardiometabolic risk factors in children.
Conclusion: Metabolic syndrome, greater waist circumference, and higher body mass index were more prevalent in children of TPO-Ab-positive mothers, indicating an adverse cardiovascular health profile.

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Cardiovascular Risk Factors Accelerate Progression of Vascular Aging in the General Population: Results From the CRAVE Study (Cardiovascular Risk Factors Affecting Vascular Age).

Terentes-Printzios D, Vlachopoulos C, Xaplanteris P, Ioakeimidis N, Aznaouridis K, Baou K, Kardara D, Georgiopoulos G, Georgakopoulos C, Tousoulis D.

Vascular aging, as assessed by structural and functional arterial properties, is an independent predictor of cardiovascular risk. We hypothesized that the number of cardiovascular risk factors determines the progression of vascular aging. One hundred forty-two subjects (mean age 51.9 years, 94 men) without established cardiovascular disease were investigated in 2 examinations over a 2-year period. Subjects were classified at baseline according to their number of risk factors (from 0 to 2 and more). Subjects had determinations of carotid-femoral pulse wave velocity, aortic augmentation index, brachial flow-mediated dilatation, and common carotid intima-media thickness and their annual absolute changes were calculated. Subjects with more risk factors had a gradual higher annual progression of pulse wave velocity (0.092 m/s/y for 0, 0.152 m/s/y for 1, and 0.352 m/s/y for 2 and more; P=0.007). Patients with both hypertension and dyslipidemia have 4× higher annual progression rate compared with subjects without these risk factors (0.398 m/s/y versus 0.102 m/s/y). When only subjects 55 years old and under were considered, the progression rate of augmentation index was higher in subjects with more risk factors (1.15%/y versus 1.50%/y versus 2.99%/y, respectively; P=0.037). No association was found with the annual change of flow-mediated dilatation or carotid intima-media thickness. In the general population, increasing number of risk factors is associated with accelerated deterioration of specific indices of vascular aging, such as pulse wave velocity and augmentation index; in contrast, flow-mediated dilatation and carotid intima-media thickness are insensitive to such changes. Accordingly, the former may be more useful for gauging vascular aging.

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Accuracy of Cardiovascular Risk Prediction Varies by Neighborhood Socioeconomic Position: A Retrospective Cohort Study.

Dalton JE, Perzynski AT, Zidar DA, Rothberg MB, Coulton CJ, Milinovich AT, Einstadter D, Karichu JK, Dawson NV.

Comment in

Ann Intern Med. 2017 Oct 3;167(7):511-512.

Background: Inequality in health outcomes in relation to Americans' socioeconomic position is rising.

Objective: First, to evaluate the spatial relationship between neighborhood disadvantage and major atherosclerotic cardiovascular disease (ASCVD)-related events; second, to evaluate the relative extent to which neighborhood disadvantage and physiologic risk account for neighborhood-level variation in ASCVD event rates.

Design: Observational cohort analysis of geocoded longitudinal electronic health records.

Setting: A single academic health center and surrounding neighborhoods in northeastern Ohio.

Patients: 109 793 patients from the Cleveland Clinic Health System (CCHS) who had an outpatient lipid panel drawn between 2007 and 2010. The date of the first qualifying lipid panel served as the study baseline.

Measurements: Time from baseline to the first occurrence of a major ASCVD event (myocardial infarction, stroke, or cardiovascular death) within 5 years, modeled as a function of a locally derived neighborhood disadvantage index (NDI) and the predicted 5-year ASCVD event rate from the Pooled Cohort Equations Risk Model (PCERM) of the American College of Cardiology and American Heart Association. Outcome data were censored if no CCHS encounters occurred for 2 consecutive years or when state death data were no longer available (that is, from 2014 onward).

Results: The PCERM systematically underpredicted ASCVD event risk among patients from disadvantaged communities. Model discrimination was poorer among these patients (concordance index [C], 0.70 [95% CI, 0.67 to 0.74]) than those from the most affluent communities (C, 0.80 [CI, 0.78 to 0.81]). The NDI alone accounted for 32.0% of census tract-level variation in ASCVD event rates, compared with 10.0% accounted for by the PCERM.

Limitations: Patients from affluent communities were overrepresented. Outcomes of patients who received treatment for cardiovascular disease at Cleveland Clinic were assumed to be independent of whether the patients came from a disadvantaged or an affluent neighborhood.

Conclusion: Neighborhood disadvantage may be a powerful regulator of ASCVD event risk. In addition to supplemental risk models and clinical screening criteria, population-based solutions are needed to ameliorate the deleterious effects of neighborhood disadvantage on health outcomes.

Primary Funding Source: The Clinical and Translational Science Collaborative of Cleveland and National Institutes of Health.

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Alcohol Use and Cardiovascular Disease Risk in Patients With Nonalcoholic Fatty Liver Disease.

VanWagner LB, Ning H, Allen NB, Ajmera V, Lewis CE, Carr JJ, Lloyd-Jones DM, Terrault NA, Siddique J.

BACKGROUND & AIMS: Cardiovascular disease (CVD) is the leading cause of death among patients with nonalcoholic fatty liver disease (NAFLD). Moderate drinking (vs abstinence) is associated with lower risk of CVD in the general population. We assessed whether alcohol use is associated with CVD risk in patients with NAFLD.
METHODS: We analyzed data from participants in the Coronary Artery Risk Development in Young Adults longitudinal cohort study of 5115 black and white young adults, 18-30 years old, recruited from 4 cities in the United States from 1985 through 1986. Participants self-reported alcohol use at study entry and then again after 15, 20, and 25 years. At year 25 (2010-2011), participants underwent computed tomography examination of the thorax and abdomen and tissue Doppler echocardiography with myocardial strain measured by speckle tracking. Coronary artery calcification was defined as an Agatston score above 0. NAFLD was defined as liver attenuation <51 Hounsfield Units after exclusions. Drinkers reported 1-21 (men) or 1-14 (women) standard drinks/week at years 15, 20, or 25. Nondrinkers reported no alcohol use at years 15, 20, and 25.
RESULTS: Of the 570 participants with NAFLD (mean age, 50 years; 54% black; 46% female), 332 (58%) were drinkers; significantly higher proportions of drinkers were white, male, and with higher levels of education compared with nondrinkers ($P < .05$ for all). Higher proportions of drinkers had obesity, diabetes, and metabolic syndrome compared with nondrinkers ($P < .01$). There was no difference in liver attenuation between groups ($P = .12$). After multivariable adjustment, there was no association between alcohol use and CVD risk factors (diabetes, hypertension, hyperlipidemia) or subclinical CVD measures (coronary artery calcification, early transmitral velocity/late (atrial) transmitral velocity (E/A) ratio, global longitudinal strain).
CONCLUSIONS: In a population-based sample of individuals with NAFLD in midlife, prospectively assessed alcohol use is not associated with significant differences in risk factors for CVD or markers of subclinical CVD. In contrast to general population findings, alcohol use may not reduce the risk of CVD in patients with NAFLD.

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PMCID: PMC5669829 [Available on 2018-11-01]
PMID: 28802566

Am J Epidemiol. 2017 Oct 1;186(7):815-823.

Primary Cardiovascular Disease Risk Factors Predicted by Poor Working Conditions in the GAZEL Cohort.

Meneton P, Lemogne C, Herquelot E, Bonenfant S, Czernichow S, Ménard J, Goldberg M, Zins M.

The mechanisms by which work environment might influence cardiovascular disease(CVD) risk are still a matter of debate. In particular, the involvement of the main behavioral and clinical risk factors and their relationships with working conditions are not always clear, despite an abundant body of literature. Most studies have investigated the impact of a limited number of characteristics of the work environment on the occurrence of 1 or a few risk factors. In contrast, in this study we used a global approach in which 30 objective and subjective indicators of working conditions were tested as predictors of 9 modifiable CVD risk factors in a well-characterized cohort of 20,625 middle-aged French workers who were followed from the 1990s until they retired or until December 31, 2013. The incidence of 3 CVD risk factors (obesity, sleep complaints, and depression) was predicted by a large number of indicators of working conditions in both age- and sex-adjusted and multivariate-adjusted Cox regression models, whatever the significance threshold retained. These results suggest the existence of close relationships between a poor work environment and a higher risk of developing obesity, sleep complaints, or depression. These risk factors may contribute to increased CVD risk not only when workers are exposed to poor working conditions but also after retirement, as predictors of the appearance of other risk factors.

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PMID: 28525584

Heart. 2017 Nov;103(22):1780-1787.

Aerobic fitness, muscular strength and obesity in relation to risk of heart failure.

Crump C, Sundquist J, Winkleby MA, Sundquist K.

OBJECTIVE: Low physical fitness and obesity have been associated with higher risk of developing heart failure (HF), but their interactive effects are unknown. Elucidation of interactions among these common modifiable factors may help facilitate more effective primary prevention.
METHODS: We conducted a national cohort study to examine the interactive effects of aerobic fitness, muscular strength and body mass index (BMI) among 1 330 610 military conscripts in Sweden during 1969-1997 (97%-98% of all 18-year-old men) on risk of HF identified from inpatient and outpatient diagnoses through 2012 (maximum age 62 years).
RESULTS: There were 11 711 men diagnosed with HF in 37.8 million person-years of follow-up. Low aerobic fitness, low muscular strength and obesity were independently associated with higher risk of HF, after adjusting for each other, socioeconomic factors, other chronic diseases and family history of HF. The combination of low aerobic fitness and low muscular strength (lowest vs highest tertiles) was associated with a 1.7-fold risk of HF (95% CI 1.6 to 1.9; p<0.001; incidence rates per 100 000 person-years, 43.2 vs 10.8). These factors had positive additive and multiplicative interactions (p<0.001) and were associated with increased risk of HF even among men with normal BMI.
CONCLUSIONS: Low aerobic fitness, low muscular strength and obesity at the age of 18 years were independently associated with higher risk of HF in adulthood, with interactive effects between aerobic fitness and muscular strength. These findings suggest that early-life interventions may help reduce the long-term risk of HF and should include both aerobic fitness and muscular strength, even among persons with normal BMI.

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PMID: 28500243

J Clin Endocrinol Metab. 2017 Nov 1;102(11):4184-4190.

Maternal Thyroid Antibodies Associates With Cardiometabolic Risk Factors in Children at the Age of 16.

Heikkinen AL, Päkkilä F, Hartikainen AL, Vääräsmäki M, Männistö T, Suvanto E.

Context and Objective: The objective of this study was to determine the effects of maternal thyroid dysfunction or antibodies during pregnancy on the cardiometabolic risk factors in children.
Design, Setting, and Participants: This prospective population-based cohort study, Northern Finland Birth Cohort 1986, included all pregnancies within a year in the area. Maternal serum samples were collected before the 20th week of gestation and analyzed for thyrotropin, free T4, thyroid-peroxidase antibodies (TPO-Abs), and thyroglobulin antibodies (Tg-Abs). Cardiometabolic risk factors in children at the age of 16 years were evaluated via blood sampling and clinical examination. Data were available for 3229 to 4176 mother-child pairs.
Main Outcome Measures: Waist circumference, blood pressure, lipids and lipoproteins, and insulin resistance were measured. Odds ratios (ORs) with 95% confidence intervals (CIs) of cardiometabolic risk factors in children with and without mothers with thyroid dysfunction or antibodies were calculated with logistic regression and adjusted for covariates.
Results: Children of TPO-Ab-positive mothers had higher odds of metabolic syndrome (OR, 2.57; 95%, CI 1.26 to 5.25) and waist circumference indicative of metabolic syndrome (OR, 1.69; 95% CI, 1.14 to 2.50). They were also more likely to be overweight or obese (OR, 1.56; 95% CI, 1.04 to 2.34). Maternal thyroid dysfunction or Tg-Ab positivity did not associate with cardiometabolic risk factors in children.
Conclusion: Metabolic syndrome, greater waist circumference, and higher body mass index were more prevalent in children of TPO-Ab-positive mothers, indicating an adverse cardiovascular health profile.

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PMID: 28945847

J Intern Med. 2017 Oct;282(4):332-339.

Alcohol consumption, cigarette smoking and incidence of aortic valve stenosis.

Larsson SC, Wolk A, Bäck M.

BACKGROUND: Alcohol consumption and cigarette smoking are modifiable lifestyle factors with important impact on public health. It is unclear whether these factors influence the risk of aortic valve stenosis (AVS).

OBJECTIVE: To investigate the associations of alcohol consumption and smoking, including smoking intensity and time since cessation, with AVS incidence in two prospective cohorts.

METHODS: This analysis was based on data from the Swedish Mammography Cohort and the Cohort of Swedish Men, comprising 69 365 adults without cardiovascular disease at baseline. Participants were followed for AVS incidence and death by linkage to the Swedish National Patient and Causes of Death Registers. Hazard ratios (HR) with 95% confidence intervals (CI) were estimated by Cox proportional hazards regression.

RESULTS: Over a mean follow-up of 15.3 years, 1249 cases of AVS (494 in women and 755 in men) were recorded. Compared with never drinkers of alcohol (lifelong abstainers), the risk of AVS was significantly lower in current light drinkers (1-6 drinks per week [1 drink = 12 g alcohol]; multivariable HR 0.82; 95% CI: 0.68-0.99). The risk of AVS increased with increasing smoking intensity. Compared with never smokers, the HR was 1.46 (95% CI: 1.16-1.85) in current smokers of ≥30 pack-years. Former smokers who had quit smoking 10 or more years previously had similar risk for AVS as never smokers.

CONCLUSIONS: This study suggests that current light alcohol consumption is associated with a lower risk of AVS, and indicates that the association between smoking and AVS risk is reversible.

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Remnant cholesterol and myocardial infarction in normal weight, overweight, and obese individuals from the Copenhagen General Population Study.

Varbo A, Freiberg JJ, Nordestgaard BG.

Objective: To investigate whether high remnant cholesterol is associated with high myocardial infarction risk, independent of whether an individual is normal weight, overweight, or obese.

Study design: The Copenhagen General Population Study is a prospective study of the Danish general population; the current data relate to 2003 to 2016. Follow-up data were obtained in individuals re-invited approximately 10 years after the initial visit, starting in 2016.

Study population: Data from 106,216 adults, mean age 58 years, 55% women were included: median BMI was 26 kg/m2 (interquartile range [IQR] 23–28 kg/m2) and median calculated remnant cholesterol concentration was 0.6 mmol/L (IQR, 0.4–0.9 mmol/L) [23 mg/dL (15–35 mg/dL)]. Overall, 902 individuals had a BMI <18.5 kg/m2 (underweight), 45,926 had a BMI between 18.5 and 24.9 kg/m2 (normal weight), 42,319 had a BMI between 25 and 29.9 kg/m2 (overweight), and 17,069 had a BMI ≥30 kg/m2 (obese).

Efficacy variables: The primary outcome was MI, determined by reviewing all hospital admissions and diagnoses entered in the national Danish Patient Registry and all causes of death entered in the national Danish Causes of Death Registry.

Remnant cholesterol was a calculated variable (defined as total cholesterol minus high-density lipoprotein cholesterol minus low-density lipoprotein cholesterol) in the main analysis; directly measured remnant cholesterol (i.e. triglyceride-rich lipoprotein cholesterol) was also measured by a newly developed homogenous automated assay.

Methods: The continuous association between calculated remnant cholesterol concentrations and BMI was evaluated by polynomial regression and P values were estimated by a linear regression of calculated remnant cholesterol and BMI, including only individuals with BMI of 18.5 to 35 kg/m2 (where the association was graphically linear). The association between calculated remnant cholesterol and BMI was also estimated by median concentrations with IQRs of remnant cholesterol across BMI deciles.

Hazard ratios for MI were estimated using Cox proportional hazards regression models adjusted for age. Individuals with an MI before study entry were excluded. Interactions between calculated remnant cholesterol and BMI on risk of MI were tested using a 2-factor interaction term, remnant cholesterol*BMI on continuous scales and in groups, in the multivariable adjusted model. Results were compared with a multivariable adjusted model without the interaction term using a likelihood ratio test.

Results: Median (IQR) remnant cholesterol for each weight category is summarized in Table 1.

Table 1. Median remnant cholesterol for each weight category

	Underweight	Normal weight	Overweight	Obese
mg/dL	15 (12–21)	19 (14–27)	27 (19–39)	33 (24–46)

Remnant cholesterol was positively associated with BMI until reaching a plateau of approximately 1 mmol/L (39 mg/dL) at BMI >35 kg/m2.

Over a follow-up of up to 11 years, 1,565 individuals experienced a MI. High remnant cholesterol was consistently associated with about 2-fold increase in MI risk in individuals who were normal weight, overweight or obese (Table 2).

Table 2. Comparison of MI risk in individuals with elevated remnant cholesterol (≥1.5 mmol/L or 58 mg/dL) versus those with values <0.5 mmol/L, by weight category

	Normal weight	Overweight	Obese
Hazard ratio (95% CI)	2.0 (1.3–3.2)	1.9 (1.4 –2.6)	2.3 (1.4 –3.5

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Nonfasting triglycerides, low-density lipoprotein cholesterol, and heart failure risk. Two cohort studies of 113 554 individuals.

Varbo A, Nordestgaard BG.

Objective: To investigate whether high concentrations of nonfasting triglycerides and LDL-C are associated with higher risk of heart failure in the general population.
Study design: Two prospective observational association studies
Study population: Data from 103,860 individuals from the Copenhagen General Population Study (55% women, mean age 58 years) and 9,694 from the Copenhagen City Heart Study (56% women, mean age 60 years) were included in this analysis. These individuals had baseline measurements for nonfasting triglycerides and LDL-C.
Efficacy variables: Onset of heart failure, defined by the International Classification of Diseases (ICD) Version 8: codes 427.09-427.11, and ICD Version 10: codes I50.0-I50.9. This was collected from 1977 to 2014 by reviewing all hospital admissions and diagnoses entered in the national Danish Patient Registry and all causes of death entered in the national Danish Causes of Death Registry.
Methods: Individuals were categorized based on levels of nonfasting triglycerides and LDL-C using clinically meaningful cutpoints, i.e. for triglycerides: <1 mmol/L (88 mg/dL), 1-1.99 mmol/L (88-175 mg/dL), 2-2.99 mmol/L (176-263 mg/dL), 3-3.99 mmol/L (264-351 mg/dL), 4-4.99 mmol/L (352-439 mg/dL), and ≥5 mmol/L (440 mg/dL) and for LDL-C: <3 mmol/L (116 mg/dL), 3-3.99 mmol/L (116-154 mg/dL), 4-4.99 mmol/L (155-193 mg/dL), and ≥5 mmol/L (193 mg/dL).
Hazard ratios were estimated with Cox proportional hazards regression models with age as the time scale; individuals with heart failure before study entry were excluded. Multivariable adjustment was made for age, sex, hypertension, lipid-lowering therapy, smoking, and atrial fibrillation.
Main results: Median follow-up time was 6 years (range: 0-11 years) in the Copenhagen General Population Study, and 19 years (range: 0-23 years) in the Copenhagen City Heart Study. During this time 3,593 individuals were diagnosed with heart failure.
In multivariable adjusted analysis of the Copenhagen General Population Study, stepwise higher nonfasting triglycerides were associated with a higher risk of heart failure. While an association between stepwise higher LDL-C and heart failure risk was observed in age and sex-adjusted analyses, this association was not evident after multivariable adjustment
Results were independently confirmed in the Copenhagen City Heart Study, with multivariable adjusted hazard ratios ranging from 1.28 (95% CI, 0.93–1.75) for nonfasting triglycerides of 1-1.99 mmol/L to 2.33 (1.22–4.45) for nonfasting triglycerides ≥5 mmol/L when compared with individuals with nonfasting triglycerides <1 mmol/L.

Mediation analyses showed that 34% (95% CI, 26%–49%) of the risk of heart failure from nonfasting triglycerides could be explained by ischaemic heart disease, 22% (95% CI, 16%–32%) by myocardial infarction, and 13% (95% CI, 9%–18%) by ischaemic heart disease without myocardial infarction (mainly angina pectoris).

Conclusion: Stepwise higher concentrations of nonfasting triglycerides were associated with stepwise higher risk of heart failure; however, concentrations of LDL-C were not associated with risk of heart failure in the general population.