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

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Am J Clin Nutr. 2015 Mar;101(3):440-8.

Is complying with the recommendations of sodium intake beneficial for health in individuals at high cardiovascular risk? Findings from the PREDIMED study.

Merino J(1), Guasch-Ferré M(1), Martínez-González MA(1), Corella D(1), Estruch R(1), Fitó M(1), Ros E(1), Arós F(1), Bulló M(1), Gómez-Gracia E(1), Moñino M(1), Lapetra J(1), Serra-Majem L(1), Razquin C(1), Buil-Cosiales P(1), Sorlí JV(1), Muñoz MA(1), Pintó X(1), Masana L(1), Salas-Salvadó J(1).

BACKGROUND: Excess sodium intake is associated with high blood pressure, a major risk factor for cardiovascular disease (CVD). It is unknown whether decreasing sodium intake to <2300 mg/d has an effect on CVD or all-cause mortality.
OBJECTIVE: The objective was to assess whether reductions in sodium intake to <2300 mg/d were associated with either an increased or a decreased risk of fatal and nonfatal CVD and all-cause mortality.
DESIGN: This observational prospective study of the PREvención con DIeta MEDiterránea (PREDIMED) trial included 3982 participants at high CVD risk. Sodium intake was evaluated with a validated food-frequency questionnaire and categorized as low (<1500 mg/d), intermediate (≥1500 to ≤2300 mg/d), high (>2300 to ≤3400 mg/d), or very high (>3400 mg/d). Subsequently, 1-y and 3-y changes in sodium intake were calculated. Multivariate relative risks were assessed by using Cox proportional hazards ratios. Marginal structural models with inverse probability weighting were used to test the effect of changes in sodium intake and the Mediterranean diet (MedDiet).
RESULTS: We documented 125 CVD events and 131 deaths after a 4.8-y median follow-up. Sodium intake <2300 mg/d was associated with a lower risk of all-cause mortality: 48% (HR: 0.52; 95% CI: 0.30, 0.91; P = 0.02) and 49% (HR: 0.51; 95% CI: 0.26, 0.98; P = 0.04) after 1 and 3 y, respectively. Increasing sodium intake after 1 y was associated with a 72% (HR: 1.72; 95% CI: 1.01, 2.91; P = 0.04) higher risk of CVD events. The incidence rate of CVD was reduced for those who reduced their sodium intake and were randomly assigned to MedDiet interventions [4.1/10,000 (95% CI: 3.1, 8.0) compared with 4.4/10,000 (95% CI: 2.7, 12.4) person-years; P = 0.002].
CONCLUSIONS: Decreasing sodium intake to <2300 mg/d was associated with a reduced risk of all-cause mortality, whereas increasing the intake to >2300 mg/d was associated with a higher risk of CVD. Our observational data suggest that sodium intake <2300 mg/d was associated with an enhanced beneficial effect of the MedDiet on CVD. These results should be interpreted with caution, and other confirmatory studies are necessary.

PMID: 25733627 [PubMed - indexed for MEDLINE]

Am Heart J. 2015 Mar;169(3):387-395.e3.

Implications of the new American College of Cardiology/American Heart Association cholesterol guidelines for primary atherosclerotic cardiovascular disease event prevention in a multi ethnic cohort: Multi-Ethnic Study of Atherosclerosis (MESA).

Yeboah J(1), Sillau S(2), Delaney JC(2), Blaha MJ(3), Michos ED(3), Young R(2), Qureshi WT(4), McClelland R(2), Burke GL(5), Psaty BM(6), Herrington DM(4).

BACKGROUND: The impact of replacing the National Cholesterol Education Program (NCEP)/Adult Treatment Program (ATP) III cholesterol guidelines with the new 2013 American College of Cardiology (ACC)/American Heart Association (AHA) guidelines for primary prevention of cardiovascular disease is unclear.

METHODS: We used risk factor and 10-year clinical event rate data from MESA, combined with estimates of efficacy of moderate and high-intensity statin therapy from meta-analyses of statin primary prevention trials to estimate (a) the change in number of subjects eligible for drug therapy and (2) the anticipated reduction in atherosclerotic cardiovascular disease (ASCVD) events and increment in type 2 diabetes mellitus (T2DM) associated with the change in cholesterol guidelines.

RESULTS: Of the 6,814 MESA participants, 5,437 were not on statins at baseline and had complete data for analysis (mean age 61.4±10.3). Using the NCEP/ATP III guidelines, 1,334 (24.5%) would have been eligible for statin therapy compared with 3,015 (55.5%) under the new ACC/AHA guidelines. Among the subset of newly eligible, 127/1,742 (7.3%) had an ASCVD event during 10years of follow-up. Assuming 10years of moderate-intensity statin therapy, the estimated absolute reduction in ASCVD events for the newly eligible group was 2.06% (number needed to treat [NNT] 48.6) and the estimated absolute increase in T2DM was 0.90% (number needed to harm [NNH] 110.7). Assuming 10years of high-intensity statin therapy, the corresponding estimates for reductions in ASCVD and increases in T2DM were as follows: ASCVD 2.70% (NNT 37.5) and T2DM 2.60% (NNH 38.6). The estimated effects of moderate-intensity statins on 10-year risk for ASCVD and T2DM in participants eligible for statins under the NCEP/ATP III were as follows: 3.20% (NNT 31.5) and 1.06% (NNH 94.2), respectively.

CONCLUSION: Substituting the NCEP/ATP III cholesterol guidelines with the 2013 ACC/AHA cholesterol guidelines in MESA more than doubled the number of participants eligible for statin therapy. If the new ACC/AHA cholesterol guidelines are adopted and extend the primary prevention population eligible for treatment, the risk-benefit profile is much better for moderate-intensity than high-intensity statin treatment.

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PMID: 25728729 [PubMed - indexed for MEDLINE]

Am J Cardiol. 2015 Mar 1;115(5):557-62.

Relationship between serum low-density lipoprotein cholesterol and in-hospital mortality following acute myocardial infarction (the lipid paradox).

Reddy VS(1), Bui QT(2), Jacobs JR(3), Begelman SM(3), Miller DP(4), French WJ(2); Investigators of National Registry of Myocardial Infarction (NRMI) 4b–5.

Lipoprotein levels are currently recognized as independent risk factors for long-term cardiovascular events after acute myocardial infarction (AMI). During the acute-phase reaction after AMI, previous studies have reported trends of decreased low-density lipoprotein cholesterol (LDL-C), increased triglycerides, and variable high-density lipoprotein cholesterol (HDL-C) levels. However, the association between LDL-C and HDL-C levels and in-hospital mortality has not been well established following AMI. The relationship between lipid levels and in-hospital all-cause mortality in 115,492 patients hospitalized for AMI (July 2002 to December 2006), registered in the National Registry of Myocardial Infarction (NRMI) 4b-5, was evaluated using multivariable-adjusted logistic regression models. Mean LDL-C was 104 ± 38, HDL-C was 41 ± 14, and triglycerides 143 ± 83 mg/dl. Compared with the lowest quartile of LDL-C (<77 mg/dl), the risk of in-hospital mortality in the second to fourth quartiles was decreased (adjusted odds ratio 0.79, 0.80, and 0.85, respectively). For HDL-C, only those in the lowest quartile (<31 mg/dl) had higher risk of in-hospital mortality (odds ratio 1.20) compared with the highest quartile (≥47 mg/dl). Results from NRMI 4b-5 suggest a lipid paradox, with lower LDL-C levels associated with increased risk of in-hospital mortality, contrary to findings outside the acute setting. Consistent with previous analyses, lowest HDL-C levels were associated with increased in-hospital mortality. In conclusion, further explorations of the relationship between very low levels of LDL-C, myocardial necrosis, and subsequent adverse cardiovascular events are warranted.

PMID: 25727079 [PubMed - indexed for MEDLINE]

Anesth Analg. 2015 Mar;120(3):543-53.

Proposed research plan for the derivation of a new Cardiac Risk Index.

Biccard B(1).

Comment in
Anesth Analg. 2015 Mar;120(3):515-8.

The Revised Cardiac Risk Index (RCRI) was incorporated into the American College of Cardiology/American Heart Association (ACC/AHA) recommendations for the preoperative evaluation of the cardiac patient for noncardiac surgery. The purpose of this review was to analyze studies on cardiovascular clinical risk prediction that had used the previous "standard best" model, the RCRI, as

a comparator. This review aims to determine whether modification of the current risk factors or adoption of other risk factors or other risk indices would improve upon the discrimination of cardiac risk prediction when compared with the RCRI. This is necessary because recent risk prediction models have shown better discrimination for major adverse cardiac events, and the pre-eminence of the RCRI is now in question. There is now a need for a new "best standard" cardiovascular risk prediction model to supersede the RCRI. This is desirable because it would: (1) allow for a global standard of cardiovascular risk assessment; (2) provide a standard comparator in all risk prediction research; (3) result in comparable data collection; and (4) allow for individual patient data meta-analyses. This should lead to continued progress in cardiovascular clinical risk prediction. A review of the current evidence suggests that to improve the preoperative clinical risk stratification for adverse cardiac events, a new risk stratification model be built that maintains the clinical risk factors identified in the RCRI, with the following modifications: (1) additional glomerular filtration rate cut points (as opposed to a single creatinine cut point); (2) age; (3) a history of peripheral vascular disease; (4) functional capacity; and (5) a specific surgical procedural category. One would expect a substantial improvement in the discrimination of the RCRI with this approach. Although most noncardiac surgeries will benefit from a standard "generic" cardiovascular risk prediction model, there are data to suggest that patients with human immunodeficiency virus disease who are undergoing vascular surgery may benefit from specific cardiovascular risk prediction models.

PMID: 25695572 [PubMed - indexed for MEDLINE]

Circulation. 2015 Feb 24;131(8):721-9

Frequent physical activity may not reduce vascular disease risk as much as moderate activity: large prospective study of women in the United Kingdom.

Armstrong ME(1), Green J(2), Reeves GK(2), Beral V(2), Cairns BJ(2); Million Women Study Collaborators.

Comment in
Circulation. 2015 Feb 24;131(8):692-4.

BACKGROUND: Although physical activity has generally been associated with reduced risk of vascular disease, there is limited evidence about the effects of the frequency and duration of various activities on the incidence of particular types of vascular disease.
METHODS AND RESULTS: In 1998, on average, 1.1 million women without prior vascular disease reported their frequency of physical activity and many other personal characteristics. Three years later, they were asked about hours spent walking, cycling, gardening, and housework each week. Women were followed by record linkage to National Health Service cause-specific hospital admissions and

death records. Cox regression was used to calculate adjusted relative risks for first vascular events in relation to physical activity. During an average of 9 years follow-up, 49,113 women had a first coronary heart disease event, 17,822 had a first cerebrovascular event, and 14,550 had a first venous thromboembolic event. In comparison with inactive women, those reporting moderate activity had significantly lower risks of all 3 conditions (P<0.001 for each). However, women reporting strenuous physical activity daily had higher risks of coronary heart disease (P=0.002), cerebrovascular disease (P<0.001), and venous thromboembolic events (P<0.001) than those reporting doing such activity 2 to 3 times per week. Risks did not differ between hemorrhagic and ischemic stroke, or between venous thromboembolic events with or without pulmonary embolism.
CONCLUSIONS: Moderate physical activity is associated with a lower risk of coronary heart disease, venous thromboembolic event, and cerebrovascular disease than inactivity. However, among active women, there is little to suggest progressive reductions in risk of vascular diseases with increasing frequency of activity.

PMID: 25688148 [PubMed - indexed for MEDLINE]

J Am Coll Cardiol. 2015 Feb 24;65(7):635-42.

Should atrial fibrillation patients with 1 additional risk factor of the CHA2DS2-VASc score (beyond sex) receive oral anticoagulation?

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Comment in
J Am Coll Cardiol. 2015 Feb 24;65(7):643-4.

BACKGROUND: Although the CHA2DS2-VASc (congestive heart failure, hypertension, age 75 years or older, diabetes mellitus, previous stroke or transient ischemic attack, vascular disease, age 65 to 74 years, female) score is recommended by both American and European guidelines for stroke risk stratification in atrial fibrillation (AF), the treatment recommendations for a CHA2DS2-VASc score of 1 are less clear.
OBJECTIVES: This study aimed to investigate the risk of ischemic stroke in patients with a single additional stroke risk factor (i.e., CHA2DS2-VASc score = 1 [males] or 2 [females]) and the impact of different component risk factors.
METHODS: We used the National Health Insurance Research Database in Taiwan. Among 186,570 AF patients not on antiplatelet or anticoagulant therapy, we evaluated males with a CHA2DS2-VASc score of 1 and females with a CHA2DS2-VASc score of 2. The clinical endpoint was the occurrence of ischemic stroke. RESULTS: Among 12,935 male AF patients with a CHA2DS2-VASc score of 1,

1,858 patients (14.4%) experienced ischemic stroke during follow-up (5.2 ± 4.3 years), with an annual stroke rate of 2.75%. Ischemic stroke risk ranged from 1.96%/year for men with vascular disease to 3.50%/year for those 65 to 74 years of age. For 7,900 females with AF and a CHA2DS2-VASc score of 2, 14.9% experienced ischemic stroke for an annual stroke rate of 2.55%. Ischemic stroke risk increased from 1.91%/year for women with hypertension to 3.34%/year for those 65 to 74 years of age.
CONCLUSIONS: Not all risk factors in CHA2DS2-VASc score carry an equal risk, with age 65 to 74 years associated with the highest stroke rate. Oral anticoagulation should be considered for AF patients with 1 additional stroke risk factor given their high risk of ischemic stroke.

PMID: 25677422 [PubMed - indexed for MEDLINE]

Mayo Clin Proc. 2015 Feb;90(2):216-23.

The association between thromboembolic complications and blood group in patients with atrial fibrillation.

Blustin JM(1), McBane RD(1), Mazur M(1), Ammash N(1), Sochor O(2), Grill DE(3), Wysokinski WE(4).

OBJECTIVE: To determine whether blood type affects the risk of thromboembolic complications in patients with atrial fibrillation (AF).
PATIENTS AND METHODS: The Mayo Clinic electronic medical record was searched (between January 1, 2004, and December 31, 2010) to identify all patients with AF with blood group assessment. Records were analyzed for stroke, transient ischemic attack, left atrium appendage thrombus, cerebral or peripheral embolism, and hemorrhagic stroke. All events were adjusted for Congestive heart failure, Hypertension, Age >75 Years, Diabetes mellitus, and Stroke/transient ischemic attack score.
RESULTS: Of the 47,816 patients with AF, 14,462 had blood group type available (40% women; mean age, 73±12 years). These included 12,363 patients with nonvalvular atrial fibrillation (NVAF) (40% women; mean age, 73±12 years) and 2099 patients with valvular AF (41% women, mean age, 73±12 years). Within patients with NVAF, the rate of peripheral embolization was significantly lower in those with blood type O (2.0%) than in those with other blood types (3.0%; odds ratio, 0.66; 95% CI, 0.52-0.84; P<.001). Neither cerebral thromboembolic (8.1% for "O" vs 8.2% for "non-O" blood group for NVAF and 7.29% vs 7.76% for valvular AF) nor cerebral hemorrhage (2.0% each group) events rates differed by blood group.
CONCLUSION: Blood group O may be protective against peripheral cardioembolic complications of NVAF, which may relate, in part, to reduced circulating von Willebrand factor levels. Cerebral thromboembolic event rates did not differ by blood group.

PMID: 25659240 [PubMed - indexed for MEDLINE]

Medicine (Baltimore). 2015 Feb;94(5):e466..

Risk factors for venous thromboembolism after spine surgery.

Tominaga H(1), Setoguchi T, Tanabe F, Kawamura I, Tsuneyoshi Y, Kawabata N, Nagano S, Abematsu M, Yamamoto T, Yone K, Komiya S.

The efficacy and safety of chemical prophylaxis to prevent the development of deep venous thrombosis (DVT) or pulmonary embolism (PE) following spine surgery are controversial because of the possibility of epidural hematoma formation. Postoperative venous thromboembolism (VTE) after spine surgery occurs at a frequency similar to that seen after joint operations, so it is important to identify the risk factors for VTE formation following spine surgery. We therefore retrospectively studied data from patients who had undergone spinal surgery and developed postoperative VTE to identify those risk factors. We conducted a retrospective clinical study with logistic regression analysis of a group of 80 patients who had undergone spine surgery at our institution from June 2012 to August 2013. All patients had been screened by ultrasonography for DVT in the lower extremities. Parameters of the patients with VTE were compared with those without VTE using the Mann-Whitney U-test and Fisher exact probability test. Logistic regression analysis was used to analyze the risk factors associated with VTE. A value of $P<0.05$ was used to denote statistical significance. The prevalence of VTE was 25.0% (20/80 patients). One patient had sensed some incongruity in the chest area, but the vital signs of all patients were stable. VTEs had developed in the pulmonary artery in one patient, in the superficial femoral vein in one patient, in the popliteal vein in two patients, and in the soleal vein in 18 patients. The Mann-Whitney U-test and Fisher exact probability test showed that, except for preoperative walking disability, none of the parameters showed a significant difference between patients with and without VTE. Risk factors identified in the multivariate logistic regression analysis were preoperative walking disability and age. The prevalence of VTE after spine surgery was relatively high. The most important risk factor for developing postoperative VTE was preoperative walking disability. Gait training during the early postoperative period is required to prevent VTE.

PMID: 25654385 [PubMed - indexed for MEDLINE]

Am Heart J. 2015 Feb;169(2):290-297.e1.

Changes in mid-life fitness predicts heart failure risk at a later age independent of interval development of cardiac and noncardiac risk factors: the Cooper Center Longitudinal Study.

Pandey A(1), Patel M(1), Gao A(1), Willis BL(2), Das SR(1), Leonard D(2), Drazner MH(1), de Lemos JA(1), DeFina L(2), Berry JD(3).

AIMS: Low mid-life fitness is associated with higher risk for heart failure (HF). However, it is unclear to what extent this HF risk is modifiable and mediated by the burden of cardiac and noncardiac comorbidities. We studied the effect of cardiac and noncardiac comorbidities on the association of mid-life fitness and fitness change with HF risk.
METHODS: Linking individual subject data from the Cooper Center Longitudinal Study (CCLS) with Medicare claims files, we studied 19,485 subjects (21.2% women) who survived to receive Medicare coverage from 1999 to 2009. Fitness estimated by Balke treadmill time at mean age of 49 years was analyzed as a continuous variable (in metabolic equivalents [METs]) and according to age- and sex-specific quintiles. Associations of mid-life fitness and fitness change with HF hospitalization after age of 65 years were assessed by applying a proportional hazards recurrent events model to the failure time data with each comorbidity entered as time-dependent covariates.
RESULTS: After 127,110 person years of Medicare follow-up, we observed 1,038 HF hospitalizations. Higher mid-life fitness was associated with a lower risk for HF hospitalization (hazard ratio [HR] 0.82 [0.76-0.87] per MET) after adjustment for traditional risk factors. This remained unchanged after further adjustment for the burden of Medicare-identified cardiac and noncardiac comorbidities (HR 0.83 [0.78-0.89]). Each 1 MET improvement in mid-life fitness was associated with a 17% lower risk for HF hospitalization in later life (HR 0.83 [0.74-0.93] per MET).
CONCLUSIONS: Mid-life fitness is an independent and modifiable risk factor for HF hospitalization at a later age.

PMID: 25641539 [PubMed - indexed for MEDLINE]

Mayo Clin Proc. 2015 Feb;90(2):224-51.

Testosterone therapy and cardiovascular risk: advances and controversies.

Morgentaler A, Miner MM, Caliber M, Guay AT, Khera M, Traish AM.

Comment in
Mayo Clin Proc. 2015 Feb;90(2):163-5.

Two recent studies raised new concerns regarding cardiovascular (CV) risks with testosterone (T) therapy. This article reviews those studies as well as the extensive literature on T and CV risks. A

MEDLINE search was performed for the years 1940 to August 2014 using the following key words: testosterone, androgens, human, male, cardiovascular, stroke, cerebrovascular accident, myocardial infarction, heart attack, death, and mortality. The weight and direction of evidence was evaluated and level of evidence (LOE) assigned. Only 4 articles were identified that suggested increased CV risks with T prescriptions: 2 retrospective analyses with serious methodological limitations, 1 placebo-controlled trial with few major adverse cardiac events, and 1 meta-analysis that included questionable studies and events. In contrast, several dozen studies have reported a beneficial effect of normal T levels on CV risks and mortality. Mortality and incident coronary artery disease are inversely associated with serum T concentrations (LOE IIa), as is severity of coronary artery disease (LOE IIa). Testosterone therapy is associated with reduced obesity, fat mass, and waist circumference (LOE Ib) and also improves glycemic control (LOE IIa). Mortality was reduced with T therapy in 2 retrospective studies. Several RCTs in men with coronary artery disease or heart failure reported improved function in men who received T compared with placebo. The largest meta-analysis to date revealed no increase in CV risks in men who received T and reduced CV risk among those with metabolic disease. In summary, there is no convincing evidence of increased CV risks with T therapy. On the contrary, there appears to be a strong beneficial relationship between normal T and CV health that has not yet been widely appreciated.

PMID: 25636998 [PubMed - indexed for MEDLINE]

Medicine (Baltimore). 2015 Jan;94(4):e508.

Risk score model for the assessment of coronary artery disease in asymptomatic patients with type 2 diabetes.

Park GM(1), An H, Lee SW, Cho YR, Gil EH, Her SH, Kim YH, Lee CW, Koh EH, Lee WJ, Kim MS, Lee KU, Kang JW, Lim TH, Park SW, Park SJ, Park JY.

No model has been developed to predict significant coronary artery disease (CAD) on coronary computed tomographic angiography (CCTA) in asymptomatic type 2 diabetes. Therefore, we sought to develop a model for the prediction of significant CAD on CCTA in these patients. We analyzed 607 asymptomatic patients with type 2 diabetes who underwent CCTA. The cardiac event was defined as a composite of cardiac death, nonfatal myocardial infarction, acute coronary syndrome, and coronary revascularization. Significant CAD (diameter stenosis ≥50%) in at least one coronary artery on CCTA was observed in 188 (31.0%). During the follow-up period (median 4.3 [interquartile range, 3.7-4.8] years), 71 patients had 83 cardiac events. Clinical risk factors for significant CAD were age, male gender, duration of diabetes, hypertension, current smoking, family history of premature CAD, previous history of stroke, ratio of total cholesterol to high-density lipoprotein cholesterol, and neuropathy. Using these variables, we formulated a risk score model, and the scores ranged from 0 to

17 (area under the curve=0.727, 95% confidence interval=0.714-0.739, P<0.001). Patients were categorized into low (≤3), intermediate (4-6), or high (≥7) risk group. There were significant differences between the risk groups in the probability of significant CAD (12.6% vs 29.4% vs 57.7%, P for all<0.001) and 5-year cardiac event-free survival rate (96.6%±1.5% vs 88.9%±1.8% vs 73.8%±4.1%, log-rank P for trend<0.001). This model predicts significant CAD on CCTA and has the potential to identify asymptomatic type 2 diabetes with high risk.

PMID: 25634204 [PubMed - indexed for MEDLINE]

Circulation. 2015 Feb 3;131(5):451-8.

Hyperlipidemia in early adulthood increases long-term risk of coronary heart disease.

Navar-Boggan AM(1), Peterson ED(2), D'Agostino RB Sr(2), Neely B(2), Sniderman AD(2), Pencina MJ(2).

Comment in
Circulation. 2015 Feb 3;131(5):445-7.

BACKGROUND: Many young adults with moderate hyperlipidemia do not meet statin treatment criteria under the new American Heart Association/American College of Cardiology cholesterol guidelines because they focus on 10-year cardiovascular risk. We evaluated the association between years of exposure to hypercholesterolemia in early adulthood and future coronary heart disease (CHD) risk.

METHODS AND RESULTS: We examined Framingham Offspring Cohort data to identify adults without incident cardiovascular disease to 55 years of age (n=1478), and explored the association between duration of moderate hyperlipidemia (non-high-density lipoprotein cholesterol ≥ 160 mg/dL) in early adulthood and subsequent CHD. At median 15-year follow-up, CHD rates were significantly elevated among adults with prolonged hyperlipidemia exposure by 55 years of age: 4.4% for those with no exposure, 8.1% for those with 1 to 10 years of exposure, and 16.5% for those with 11 to 20 years of exposure (P<0.001); this association persisted after adjustment for other cardiac risk factors including non-high-density lipoprotein cholesterol at 55 years of age (hazard ratio, 1.39; 95% confidence interval, 1.05-1.85 per decade of hyperlipidemia). Overall, 85% of young adults with prolonged hyperlipidemia would not have been recommended for statin therapy at 40 years of age under current national guidelines. However, among those not considered statin therapy candidates at 55 years of age, there remained a significant association between cumulative exposure to hyperlipidemia in young adulthood and subsequent CHD risk (adjusted hazard ratio, 1.67; 95% confidence interval, 1.06-2.64).

CONCLUSIONS: Cumulative exposure to hyperlipidemia in young adulthood increases the subsequent risk of CHD in a dose-dependent fashion. Adults with prolonged exposure to even moderate elevations in non-high-density lipoprotein cholesterol have elevated risk for future CHD and may benefit from more aggressive primary prevention.

PMCID: PMC4370230 [Available on 2016-02-03]
PMID: 25623155 [PubMed - indexed for MEDLINE]

Pediatrics. 2015 Feb;135(2):e405-15.

Cardiovascular risk factors in children after repeat doses of antenatal glucocorticoids: an RCT.

McKinlay CJ(1), Cutfield WS(1), Battin MR(2), Dalziel SR(3), Crowther CA(4), Harding JE(5); ACTORDS Study Group.

BACKGROUND: Treatment of women at risk for preterm birth with repeat doses of glucocorticoids reduces neonatal morbidity but could have adverse long-term effects on cardiometabolic health in offspring. We assessed whether exposure to repeat antenatal betamethasone increased risk factors for later cardiometabolic disease in children whose mothers participated in the Australasian Collaborative Trial of Repeat Doses of Corticosteroids.
METHODS: Women were randomized to betamethasone or placebo treatment, ≥ 7 days after an initial course of glucocorticoids, repeated each week that they remained at risk for preterm birth at <32 weeks' gestation. In this follow-up study, children were assessed at 6 to 8 years' corrected age for body composition, insulin sensitivity, ambulatory blood pressure, and renal function.
RESULTS: Of 320 eligible childhood survivors, 258 were studied (81%; 123 repeat betamethasone group; 135 placebo [single course] group). Children exposed to repeat antenatal betamethasone and those exposed to placebo had similar total fat mass (geometric mean ratio 0.98, 95% confidence interval [CI] 0.78 to 1.23), minimal model insulin sensitivity (geometric mean ratio 0.89, 95% CI 0.74 to 1.08), 24-hour ambulatory blood pressure (mean difference systolic 0 mm Hg, 95% CI -2 to 2; diastolic 0 mm Hg, 95% CI -1 to 1), and estimated glomerular filtration rate (mean difference 1.2 mL/min/1.73 m(2), 95% CI -3.2 to 5.6).
CONCLUSIONS: Exposure to repeat doses of antenatal betamethasone compared with a single course of glucocorticoids does not increase risk factors for cardiometabolic disease at early school age.
PMID: 25601978 [PubMed - indexed for MEDLINE]

Circulation. 2015 Jan 20;131(3):245-53.

Cumulative effect of psychosocial factors in youth on ideal cardiovascular health in adulthood: the Cardiovascular Risk in Young Finns Study.

Pulkki-Råback L(1), Elovainio M(2), Hakulinen C(2), Lipsanen J(2), Hintsanen M(2), Jokela M(2), Kubzansky LD(2), Hintsa T(2), Serlachius A(2), Laitinen T(2), Pahkala K(2), Mikkilä V(2), Nevalainen J(2), Hutri-Kähönen N(2), Juonala M(2), Viikari J(2), Raitakari OT(2), Keltikangas-Järvinen L(2).

Comment in

Circulation. 2015 Jan 20;131(3):230-1.

BACKGROUND: The American Heart Association has defined a new metric of ideal cardiovascular health as part of its 2020 Impact Goals. We examined whether psychosocial factors in youth predict ideal cardiovascular health in adulthood.

METHODS AND RESULTS: Participants were 477 men and 612 women from the nationwide Cardiovascular Risk in Young Finns Study. Psychosocial factors were measured from cohorts 3 to 18 years of age at the baseline of the study, and ideal cardiovascular health was examined 27 years later in adulthood. The summary measure of psychosocial factors in youth comprised socioeconomic factors, emotional factors, parental health behaviors, stressful events, self-regulation of the child, and social adjustment of the child. There was a positive association between a higher number of favorable psychosocial factors in youth and greater ideal cardiovascular health index in adulthood (β=0.16; P<0.001) that persisted after adjustment for age, sex, medication use, and cardiovascular risk factors in childhood (β=0.15; P<0.001). The association was monotonic, suggesting that each increment in favorable psychosocial factors was associated with improvement in cardiovascular health. Of the specific psychosocial factors, a favorable socioeconomic environment (β=0.12; P<0.001) and participants' self-regulatory behavior (β=0.07; P=0.004) were the strongest predictors of ideal cardiovascular health in adulthood.

CONCLUSIONS: The findings suggest a dose-response association between favorable psychosocial factors in youth and cardiovascular health in adulthood, as defined by the American Heart Association metrics. The effect seems to persist throughout the range of cardiovascular health, potentially shifting the population distribution of cardiovascular health rather than simply having effects in a high-risk population.

PMID: 25583139 [PubMed - indexed for MEDLINE]

Am J Cardiol. 2015 Feb 1;115(3):328-33.

Anemia and reduced kidney function as risk factors for new onset of atrial fibrillation (from the Ibaraki prefectural health study).

Xu D(1), Murakoshi N(2), Sairenchi T(3), Irie F(4), Igarashi M(1), Nogami A(5), Tomizawa T(6), Yamaguchi I(6), Yamagishi K(7), Iso H(8), Ota H(9), Aonuma K(5).

Chronic kidney disease (CKD) is a potential independent risk factor for atrial fibrillation (AF). It remains unclear whether anemia is synergistically associated with increased risk of AF onset in subjects with CKD. We evaluated the association of kidney function, hemoglobin (Hb), and their combination with new-onset AF in a population-based cohort study. We conducted a 15-year prospective cohort study of 132,250 Japanese subjects aged 40 to 79 years who participated in annual health checkups from 1993. Kaplan-Meier survival analysis was used to compare freedom from new-onset AF between groups classified by estimated glomerular filtration rate grade, Hb grade, and their combination. Cox proportional hazard model analysis was used to estimate hazard ratios (HRs) for new-onset AF. During a 13.8-year mean follow-up period, 1,232 (0.93%) subjects with new-onset AF were identified. Lower estimated glomerular filtration rate and lower Hb grades were significantly associated with a higher incidence of new-onset AF. Multivariate HRs and 95% confidence intervals (CIs) of new-onset AF were 1.38 (1.21 to 1.56) for mild CKD group, 2.56 (2.09 to 3.13) for CKD group, and 1.50 (1.24 to 1.83) for anemia group. Borderline Hb level was not significantly associated with increased risk for new-onset AF (HR 1.07, CI 0.91 to 1.25, p = 0.4284). In the model with interaction term between CKD and anemia, the risk was significantly higher (p = 0.0343 for the interaction) than that predicted by each factor independently. In conclusion, decreased kidney function and lower Hb level are associated with increased risk for new-onset AF, especially when both are present.

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Healthy lifestyle in the primordial prevention of cardiovascular disease among young women

Chomistek AK(1), Chiuve SE(2), Eliassen AH(3), Mukamal KJ(4), Willett WC(5), Rimm EB(5).

Comment in
J Am Coll Cardiol. 2015 Jan 6;65(1):52-4.

BACKGROUND: Overall mortality rates from coronary heart disease (CHD) in the United States have declined in recent decades, but the rate has plateaued among younger women. The potential for further reductions in mortality rates among young women through changes in lifestyle is unknown. OBJECTIVES: The aim of this study was to estimate the proportion of CHD cases and clinical

cardiovascular disease (CVD) risk factors among young women that might be attributable to poor adherence to a healthy lifestyle.

METHODS: A prospective analysis was conducted among 88,940 women ages 27 to 44 years at baseline in the Nurses' Health Study II who were followed from 1991 to 2011. Lifestyle factors were updated repeatedly by questionnaire. A healthy lifestyle was defined as not smoking, a normal body mass index, physical activity ≥ 2.5 h/week, television viewing ≤ 7 h/week, diet in the top 40% of the Alternative Healthy Eating Index-2010, and 0.1 to 14.9 g/day of alcohol. To estimate the proportion of CHD and clinical CVD risk factors (diabetes, hypertension, and hypercholesterolemia) that could be attributed to poor adherence to a healthy lifestyle, we calculated the population-attributable risk percent.

RESULTS: During 20 years of follow-up, we documented 456 incident CHD cases. In multivariable-adjusted models, nonsmoking, a healthy body mass index, exercise, and a healthy diet were independently and significantly associated with lower CHD risk. Compared with women with no healthy lifestyle factors, the hazard ratio for CHD for women with 6 lifestyle factors was 0.08 (95% confidence interval: 0.03 to 0.22). Approximately 73% (95% confidence interval: 39% to 89%) of CHD cases were attributable to poor adherence to a healthy lifestyle. Similarly, 46% (95% confidence interval: 43% to 49%) of clinical CVD risk factor cases were attributable to a poor lifestyle.

CONCLUSIONS: Primordial prevention through maintenance of a healthy lifestyle among young women may substantially lower the burden of CVD.

PMCID: PMC4291551 [Available on 2016-01-06]
PMID: 25572509 [PubMed - indexed for MEDLINE]

Obstet Gynecol. 2015 Jan;125(1):124-31.

Hypertensive disorders and pregnancy-related stroke: frequency, trends, risk factors, and outcomes.

Leffert LR(1), Clancy CR, Bateman BT, Bryant AS, Kuklina EV.

OBJECTIVE: To evaluate trends and associations of hypertensive disorders of pregnancy with stroke risk and test the hypothesis that hypertensive disorders of pregnancy-associated stroke results in higher rates of stroke-related complications than pregnancy-associated stroke without hypertensive disorders.

METHODS: A cross-sectional study was performed using 81,983,216 pregnancy hospitalizations from the 1994-2011 Nationwide Inpatient Sample. Rates of stroke hospitalizations with and without these hypertensive disorders were reported per 10,000 pregnancy hospitalizations. Using logistic regression, adjusted odds ratios (OR) with 95% confidence intervals were obtained.

RESULTS: Between 1994-1995 and 2010-2011, the nationwide rate of stroke with hypertensive disorders of pregnancy increased from 0.8 to 1.6 per 10,000 pregnancy hospitalizations (103%), whereas the rate without these disorders increased from 2.2 to 3.2 per 10,000 pregnancy hospitalizations (47%). Women with hypertensive disorders of pregnancy were 5.2 times more likely to have a stroke than those without. Having traditional stroke risk factors (eg, congenital heart disease, atrial fibrillation, sickle cell anemia, congenital coagulation defects) substantially increased the stroke risk among hypertensive disorders of pregnancy hospitalizations: from adjusted OR 2.68 for congenital coagulation defects to adjusted OR 13.1 for congenital heart disease. Stroke-related complications were increased in stroke with hypertensive disorders of pregnancy compared with without (from adjusted OR 1.23 for nonroutine discharge to adjusted OR 1.93 for mechanical ventilation).
CONCLUSION: Having traditional stroke risk factors substantially increased the stroke risk among hypertensive disorders of pregnancy hospitalizations. Stroke with hypertensive disorders in pregnancy had two distinctive characteristics: a greater increase in frequency since the mid-1990s and significantly higher stroke-related complication rates.
LEVEL OF EVIDENCE: III.

PMID: 25560114 [PubMed - indexed for MEDLINE]

Am J Clin Nutr. 2015 Jan;101(1):164-72.

Rice consumption and risk of cardiovascular disease: results from a pooled analysis of 3 U.S. cohorts.

Muraki I(1), Wu H(1), Imamura F(1), Laden F(1), Rimm EB(1), Hu FB(1), Willett WC(1), Sun Q(1).

BACKGROUND: Health concerns have been raised about rice consumption, which may significantly contribute to arsenic exposure. However, little is known regarding whether habitual rice consumption is associated with cardiovascular disease (CVD) risk.
OBJECTIVE: We examined prospectively the association of white rice and brown rice consumption with CVD risk.
DESIGN: We followed a total of 207,556 women and men [73,228 women from the Nurses' Health Study (1984-2010), 92,158 women from the Nurses' Health Study II (1991-2011), and 42,170 men from the Health Professionals Follow-Up Study (1986-2010)] who were free of CVD and cancer at baseline. Validated semi quantitative food-frequency questionnaires were used to assess consumption of white rice, brown rice, and other food items. Fatal and nonfatal CVD (coronary artery disease and stroke) was confirmed by medical records or self-reports.
RESULTS: During 4,393,130 person-years of follow-up, 12,391 cases of CVD were identified. After adjustment for major CVD risk factors, including demographics, lifestyle, and other dietary intakes, rice

consumption was not associated with CVD risk. The multivariable-adjuted HR of developing CVD comparing ≥5 servings/wk with <1 serving/wk was 0.98 (95% CI: 0.84, 1.14) for white rice, 1.01 (0.79, 1.28) for brown rice, and 0.99 (0.90, 1.08) for total rice. To minimize the potential impact of racial difference in rice consumption, we restricted the analyses to whites only and obtained similar results: the HRs of CVD for ≥5 servings/wk compared with <1 serving/wk were 1.04 (95% CI: 0.88, 1.22) for white rice and 1.01 (0.78, 1.31) for brown rice.
CONCLUSIONS: Greater habitual consumption of white rice or brown rice is not associated with CVD risk. These findings suggest that rice consumption may not pose a significant CVD risk among the U.S. population when consumed at current amounts. More prospective studies are needed to explore these associations in other populations.

PMCID: PMC4266886
PMID: 25527760 [PubMed - indexed for MEDLINE]

Am J Clin Nutr. 2015 Jan;101(1):144-52

Multivitamin use and cardiovascular disease in a prospective study of women.

Rautiainen S(1), Lee IM(1), Rist PM(1), Gaziano JM(1), Manson JE(1), Buring JE(1), Sesso HD(1).

BACKGROUND: Although multivitamins are widely used, there are limited prospective studies investigating their association with both long- and short-term risk of cardiovascular disease (CVD).
OBJECTIVE: The objective was to investigate how multivitamin use is associated with the long- and short-term risk of CVD.
DESIGN: A prospective cohort study was conducted of 37,193 women from the Women's Health Study aged ≥45 y and free of CVD and cancer at baseline who were followed for an average of 16.2 y. At baseline, women self-reported a wide range of lifestyle, clinical, and dietary factors. Women were categorized into 1) no current use and 2) current use of multivitamins. Duration and updated measures over the course of the follow-up to address short-term effects were also considered. Women were followed for major CVD events, including myocardial infarction (MI), stroke, and CVD death.
RESULTS: During the follow-up, 1493 incident cases of CVD [defined as myocardial infarction (MI), stroke, and CVD death] occurred. In multivariable analyses, multivitamin use compared with no use was not associated with major CVD events (HR: 1.01; 95% CI: 0.89, 1.15), MI (HR: 1.04; 95% CI: 0.84, 1.27), stroke (HR: 0.99; 95% CI: 0.83, 1.18), or CVD death (HR: 1.10; 95% CI: 0.84, 1.45). A nonsignificant inverse association was observed between baseline multivitamin use and major CVD events among women aged ≥70 y (P-interaction = 0.04) and those consuming <3 servings/d of fruit and vegetables (P-interaction = 0.01). When updating information on multivitamin use during the course of follow-up, no associations were observed for major CVD events (HR: 0.91; 95% CI: 0.82,

1.02), MI (HR: 0.89; 95% CI: 0.74, 1.06), stroke (HR: 0.91; 95% CI: 0.78, 1.06), and CVD death (HR: 0.91; 95% CI: 0.71, 1.16).
CONCLUSIONS: In this study of middle-aged and elderly women, neither baseline nor time-varying multivitamin use was associated with the long-term risk of major CVD events, MI, stroke, cardiac revascularizations, or CVD death. Additional studies are needed to clarify the role of multivitamins on CVD.

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PMID: 25527758 [PubMed - indexed for MEDLINE]

Circulation. 2015 Jan 20;131(3):237-44

Age at menarche and risks of coronary heart and other vascular diseases in a large UK cohort.

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Comment in
Circulation. 2015 Jan 20;131(3):227-9.

BACKGROUND: Early menarche has been associated with increased risk of coronary heart disease (CHD), but most studies were relatively small and could not assess risk across a wide range of menarcheal ages; few have examined associations with other vascular diseases. We examined CHD, cerebrovascular disease, and hypertensive disease risks by age at menarche in a large prospective study of UK women.
METHODS AND RESULTS: In 1.2 million women (mean±SD age, 56±5 years) without previous heart disease, stroke, or cancer, menarcheal age was reported to be 13 years by 25%, ≤10 years by 4%, and ≥17 years by 1%. After 11.6 years of follow-up, 73 378 women had first hospitalization for or death from CHD, 25 426 from cerebrovascular disease, and 249 426 from hypertensive disease. Using Cox regression, we calculated relative risks for each vascular outcome by single year of menarcheal age. The relationship was U-shaped for CHD. Compared with women with menarche at 13 years, the adjusted relative risk for CHD for menarche at ≤10 years of age was 1.27 (95% confidence interval, 1.22-1.31; P<0.0001) and for menarche at ≥17 years of age was 1.23 (95% confidence interval, 1.16-1.30; P<0.0001). U-shaped relationships were also seen for cerebrovascular and hypertensive disease, although the magnitudes of these risks for early and late menarche were smaller than those for CHD.
CONCLUSIONS: In this cohort, the relation of age at menarche to vascular disease risk was U shaped, with both early and late menarche being associated with increased risk. Associations were weaker for cerebrovascular and hypertensive disease than for CHD.

PMID: 25512444 [PubMed - indexed for MEDLINE]

Am Heart J. 2015 Jan;169(1):108-14.e7.

Cardiovascular prognosis in patients with type 2 diabetes: contribution of heart and kidney subclinical damage.

Sosner P(1), Hulin-Delmotte C(2), Saulnier PJ(3), Cabasson S(4), Gand E(5), Torremocha F(5), Piguel X(5), Miot A(6), Maréchaud R(6), Herpin D(7), Ragot S(8), Hadjadj S(9); SURDIAGENE Study Group.

BACKGROUND: Left ventricular hypertrophy (LVH) and kidney damage (abnormal urinary albumin-to-creatinine ratio [uACR] or estimated glomerular filtration rate [eGFR]) are predictive of major cardiovascular events (MACE) in patients with type 2 diabetes (T2D) but are rarely used in cardiovascular score calculators. Our study aimed to assess their respective prognostic values for MACE and the additive information they provide to score calculators.
METHODS: A total of 1298 T2D (43% women) aged 65 (SD 11) years were followed up for a median of 65 months, with MACE as a primary composite end point: cardiovascular death, nonfatal myocardial infarction, or stroke. Electrocardiogram (ECG)-derived LVH was defined using Sokolow, Gubner, and Cornell product indexes; uACR was considered as abnormal if >2.5 mg/mmol in men or >3.5 mg/mmol in women and eGFR if <60 mL/min per 1.73 m(2).
RESULTS: Urinary albumin-to-creatinine ratio was higher in subjects with electrocardiographic LVH (ECG-LVH) than in subjects without (median [interquartile range] 7.61 [43.48] and 2.56 [10.53], respectively; P < .0001). After adjustment for age, history of myocardial infarction, and peripheral artery disease, ECG-LVH and kidney damage were strong predictors for MACE (adjusted hazard ratio [1.64; 95% CI 1.23-2.20], [1.90; 95% CI 1.43-2.53], and [1.85; 95% CI 1.42-2.41] for ECG-LVH, uACR, and eGFR, respectively). Net reclassification improvement was higher with the model including both ECG-LVH and uACR than models with ECG-LVH alone (P < .0001) or uACR alone (P < .0001). In addition, using cardiovascular risk calculators (Framingham score and others), we observed an additional prognostic value of ECG-LVH for each one of them.
CONCLUSIONS: Electrocardiographic LVH is complementary to kidney damage for MACE prediction in T2D.

PMID: 25497255 [PubMed - indexed for MEDLINE]

Am J Med. 2015 Mar;128(3):297-302

Venous thromboembolism and cardiovascular risk: results from the NAVIGATOR trial.

Katz M(1), Califf RM(2), Sun JL(3), McMurray JJ(4), Thomas L(3), Lopes RD(5).

BACKGROUND: Contemporary studies suggest an association between venous thromboembolism and a higher incidence of major cardiovascular events, mostly attributed to arterial atherothrombosis. Using data from the Nateglinide and Valsartan in Impaired Glucose Tolerance Outcomes Research (NAVIGATOR) trial, we assessed the association of venous thromboembolism with major cardiovascular events.
METHODS: In NAVIGATOR, patients with impaired glucose tolerance were randomly allocated to receive valsartan or placebo and nateglinide or placebo in addition to lifestyle modification. Baseline characteristics and prior history of venous thromboembolism were assessed. After adjusting for important baseline covariates, Cox proportional hazards regression models were used to assess the association between venous thromboembolism and major cardiovascular outcomes.
RESULTS: Of the 9306 patients enrolled, 129 (1.4%) had a history of venous thromboembolism. Patients with venous thromboembolism were older, more frequently white and female, and had a higher body mass index. Patients with venous thromboembolism had higher 5-year event rates for the composite of death, myocardial infarction, and stroke, as compared with patients without venous thromboembolism (10.7% vs 5.9%; P < .001; adjusted hazard ratio 2.12; 95% confidence interval, 1.36-3.31; P = .001).
CONCLUSION: In patients with impaired glucose tolerance at high risk for cardiovascular events, the prevalence of venous thromboembolism was rare but associated with worse long-term cardiovascular outcomes, including arterial events. Venous thromboembolism is a marker of risk, and attention should be paid to this high-risk group of patients.

PMID: 25447626 [PubMed - indexed for MEDLINE]

Am J Med. 2015 Mar;128(3):219-28.

Resting heart rate: risk indicator and emerging risk factor in cardiovascular disease.

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Resting heart rate is central to cardiac output and is influenced by changes occurring in numerous diseases. It predicts longevity and cardiovascular diseases, and current evidence suggests that it is also an important marker of outcome in cardiovascular disease, including heart failure. Beta-blockers improve outcomes in heart failure; however, they have effects outside reducing heart rate. Ivabradine has demonstrated efficacy in reducing rehospitalizations and mortality in heart failure and in improving exercise tolerance and reducing angina attacks in patients with coronary artery disease, whereas

selective heart rate reduction may also prove to be beneficial in therapeutic areas outside those in which ivabradine has already demonstrated clinical efficacy. This review provides an update on the associations between heart rate and cardiovascular outcomes in various conditions, the experimental effects of heart rate reduction with ivabradine, and the potential new indications in cardiovascular disease.

PMID: 25447617 [PubMed - indexed for MEDLINE]

Heart. 2015 Feb;101(3):215-21.

Obesity related risk of sudden cardiac death in the atherosclerosis risk in communities study.

Adabag S(1), Huxley RR(2), Lopez FL(3), Chen LY(4), Sotoodehnia N(5), Siscovick D(6), Deo R(7), Konety S(4), Alonso A(3), Folsom AR(3).

Comment in
Heart. 2015 Feb;101(3):165-6.

OBJECTIVE: To examine the association of body mass index (BMI), waist circumference (WC) and waist hip ratio (WHR) with sudden cardiac death (SCD) in community dwelling individuals.
METHODS: Data from a multicentre, prospective, cohort study of 14 941 men and women (African American, and white), aged 45-64 years, participating in the Atherosclerosis Risk in Communities study was analysed. Obesity measures were assessed at baseline (1987-1989). SCD was adjudicated by a committee.
RESULTS: At enrolment mean±SD age of the participants was 54±6 years (55% female; 26% African American). During 12.6±2.5 years of follow-up, 253 SCD occurred (incidence rate 1.34/100 person-years). The association between obesity and SCD differed by smoking status (interaction p≤0.01). In models adjusting for age, sex, race, study centre and education level, SCD risk was positively associated (p<0.001) with BMI, WC and WHR in non-smokers, but not in smokers. WHR was more strongly associated with SCD in non-smokers than was BMI or WC (HR per SD increment (95% CI) 2.00 (1.65 to 2.42); 1.34 (1.15 to 1.56) and 1.49 (1.28 to 1.74), respectively). After adjustment for potential mediators (hypertension, diabetes, lipid profile, prevalent coronary heart disease, heart failure, and LV hypertrophy), non-smokers in the highest WHR category (>0.95 in women; >1.01 in men) had double the risk of SCD (HR 2.03, 95% CI 1.19 to 3.46; incidence rate 1.43/1000 person-years) versus those with normal WHR.
CONCLUSIONS: General obesity is associated with increased risk of SCD in middle-aged, non-smoking individuals, mediated by traditional cardiovascular risk factors. Central obesity, however, is independently associated with SCD by pathways that remain to be elucidated.

PMID: 25410499 [PubMed - indexed for MEDLINE]

Heart. 2015 Jan;101(1):58-64..

Heart failure risk prediction in the Multi-Ethnic Study of Atherosclerosis.

Chahal H(1), Bluemke DA(2), Wu CO(3), McClelland R(4), Liu K(5), Shea SJ(6), Burke G(7), Balfour P(8), Herrington D(8), Shi P(3), Post W(1), Olson J(9), Watson KE(10), Folsom AR(11), Lima JA(1).

Comment in
Heart. 2015 Jan;101(1):7-9.

OBJECTIVE: Heart failure (HF) is a leading cause of mortality especially in older populations. Early detection of high-risk individuals is imperative for primary prevention. The purpose of this study was to develop a HF risk model from a population without clinical cardiac disease.
METHODS: The Multi-Ethnic Study of Atherosclerosis is a multicentre observational cohort study following 6814 subjects (mean age 62±10 years; 47% men) who were free of clinical cardiovascular disease at baseline. Median follow-up was 4.7 years. HF events developed in 176 participants. Cox proportional hazards models and regression coefficients were used to determine independent risk factors and generate a 5-year risk score for incident HF. Bootstrapping with bias correction was used for internal validation.
RESULTS: Independent predictors for HF (HR, p value) were age (1.30 (1.10 to 1.50) per 10 years), male gender (2.27 (1.53 to 3.36)), current smoking (1.97 (1.15 to 3.36)), body mass index (1.40 (1.10 to 1.80) per 5 kg/m(2)), systolic blood pressure (1.10 (1.00 to 1.10) per 10 mm Hg), heart rate (1.30) (1.10 to 1.40) per 10 bpm), diabetes (2.27 (1.48 to 3.47)), N-terminal pro-B-type natriuretic peptide (NT proBNP) (2.48 (2.16 to 2.84) per unit log increment) and left ventricular mass index (1.40 (1.30 to 1.40) per 10 g/m(2)). A parsimonious model based on age, gender, body mass index, smoking status, systolic blood pressure, heart rate, diabetes and NT proBNP natriuretic peptide predicted incident HF risk with a c-statistic of 0.87.
CONCLUSIONS: A clinical algorithm based on risk factors readily available in the primary care setting can used to identify individuals with high likelihood of developing HF without pre-existing cardiac disease.

PMID: 25381326 [PubMed - indexed for MEDLINE]

Arthritis Rheumatol. 2015 Feb;67(2):381-5.

The ability of the 2013 American College of Cardiology / American Heart Association cardiovascular risk score to identify rheumatoid arthritis patients with high coronary artery calcification scores.

Kawai VK, Chung CP, Solus JF, Oeser A, Raggi P, Stein CM.

OBJECTIVE: Patients with rheumatoid arthritis (RA) have increased risk of atherosclerotic cardiovascular disease that is underestimated by the Framingham Risk Score (FRS). We undertook this study to test the hypothesis that the 2013 American College of Cardiology/American Heart Association (ACC/AHA) 10-year risk score would perform better than the FRS and the Reynolds Risk Score (RRS) in identifying RA patients known to have elevated cardiovascular risk based on high coronary artery calcification (CAC) scores.

METHODS: Among 98 RA patients eligible for risk stratification using the ACC/AHA risk score, we identified 34 patients with high CAC (defined as ≥300 Agatston units or ≥75th percentile of expected coronary artery calcium for age, sex, and ethnicity) and compared the ability of the 10-year FRS, RRS, and ACC/AHA risk scores to correctly assign these patients to an elevated risk category.

RESULTS: All 3 risk scores were higher in patients with high CAC ($P < 0.05$). The percentage of patients with high CAC correctly assigned to the elevated risk category was similar among the 3 scores (FRS 32%, RRS 32%, ACC/AHA risk score 41%) ($P = 0.223$). The C statistics for the FRS, RRS, and ACC/AHA risk score predicting the presence of high CAC were 0.65, 0.66, and 0.65, respectively.

CONCLUSION: The ACC/AHA 10-year risk score does not offer any advantage compared to the traditional FRS and RRS in the identification of RA patients with elevated risk as determined by high CAC. The ACC/AHA risk score assigned almost 60% of patients with high CAC to a low risk category. Risk scores and standard risk prediction models used in the general population do not adequately identify many RA patients with elevated cardiovascular risk.

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PMID: 25371313 [PubMed - indexed for MEDLINE]

Prog Cardiovasc Dis. 2015 Jan-Feb;57(4):324-9

Physical activity versus cardiorespiratory fitness: two (partly) distinct components of cardiovascular health?

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Physical activity (PA) and cardiorespiratory fitness (CRF) both have inverse relationships to cardiovascular (CV) morbidity and mortality. Recent position papers and guidelines have identified the important role of both of these factors in CV health. The benefits of PA and CRF in the prevention of CV disease and risk factors are reviewed. In addition, assessment methodology and utilization in the research and clinical arenas are discussed. Finally, the benefits, methodology, and utilization are compared and contrasted to better understand the two (partly) distinct components and their impact on CV health.

PMID: 25269066 [PubMed - indexed for MEDLINE]

Prog Cardiovasc Dis. 2015 Jan-Feb;57(4):306-14.

Physical activity and cardiorespiratory fitness as major markers of cardiovascular risk: their independent and interwoven importance to health status.

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The evolution from hunting and gathering to agriculture, followed by industrialization, has had a profound effect on human physical activity (PA) patterns. Current PA patterns are undoubtedly the lowest they have been in human history, with particularly marked declines in recent generations, and future projections indicate further declines around the globe. Non-communicable health problems that afflict current societies are fundamentally attributable to the fact that PA patterns are markedly different than those for which humans were genetically adapted. The advent of modern statistics and epidemiological methods has made it possible to quantify the independent effects of cardiorespiratory fitness (CRF) and PA on health outcomes. Based on more than five decades of epidemiological studies, it is now widely accepted that higher PA patterns and levels of CRF are associated with better health outcomes. This review will discuss the evidence supporting the premise that PA and CRF are independent risk factors for cardiovascular disease (CVD) as well as the interplay between both PA and CRF and other CVD risk factors. A particular focus will be given to the interplay between CRF, metabolic risk and obesity.

PMID: 25269064 [PubMed - indexed for MEDLINE]

Heart. 2015 Feb;101(3):222-9.

The validation of cardiovascular risk scores for patients with type 2 diabetes mellitus

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OBJECTIVE: Various cardiovascular prediction models have been developed for patients with type 2 diabetes. Their predictive performance in new patients is mostly not investigated. This study aims to quantify the predictive performance of all cardiovascular prediction models developed specifically for diabetes patients.
DESIGN AND METHODS: Follow-up data of 453, 1174 and 584 type 2 diabetes patients without pre-existing cardiovascular disease (CVD) in the EPIC-NL, EPIC-Potsdam and Secondary Manifestations of ARTerial disease cohorts, respectively, were used to validate 10 prediction models to estimate risk of CVD or coronary heart disease (CHD). Discrimination was assessed by the c-statistic for time-to-event data. Calibration was assessed by calibration plots, the Hosmer-Lemeshow goodness-of-fit statistic and expected to observed ratios.
RESULTS: There was a large variation in performance of CVD and CHD scores between different cohorts. Discrimination was moderate for all 10 prediction models, with c-statistics ranging from 0.54 (95% CI 0.46 to 0.63) to 0.76 (95% CI 0.67 to 0.84). Calibration of the original models was poor. After simple recalibration to the disease incidence of the target populations, predicted and observed risks were close. Expected to observed ratios of the recalibrated models ranged from 1.06 (95% CI 0.81 to 1.40) to 1.55 (95% CI 0.95 to 2.54), mainly driven by an overestimation of risk in high-risk patients.
CONCLUSIONS: All 10 evaluated models had a comparable and moderate discriminative ability. The recalibrated, but not the original, prediction models provided accurate risk estimates. These models can assist clinicians in identifying type 2 diabetes patients who are at low or high risk of developing CVD.

PMID: 25256148 [PubMed - indexed for MEDLINE]

Cancer. 2015 Jan 15;121(2):311-9.

Clinical risk factors for the development of hypertension in patients treated with inhibitors of the VEGF signaling pathway.

Hamnvik OP(1), Choueiri TK, Turchin A, McKay RR, Goyal L, Davis M, Kaymakcalan MD, Williams JS.

BACKGROUND: VEGF signaling pathway inhibitor (anti-VEGF) therapy is associated with hypertension, but little is known about predisposing clinical characteristics. This study describes the

real-world association between baseline clinical characteristics, blood pressure (BP) response, and survival in patients prescribed anti-VEGF therapies.
METHODS: Clinical data from Partners HealthCare in Massachusetts was obtained from adults treated with anti-VEGF therapies (2002-2013). Treatment-induced hypertensive response was defined as worsening of preexisting hypertension or new diagnosis of hypertension (if no prior hypertension history).
RESULTS: Data from 1120 patients with renal cell carcinoma (32.2%), hepatocellular carcinoma (11.6%), gastrointestinal stromal tumors (12.5%), and other sarcomas (15.3%) were analyzed. Most patients received sunitinib (52%), sorafenib (25.9%), or pazopanib (18%). A treatment-induced hypertensive response was identified in 49.7% of treated patients. Preexisting hypertension, present in 65.4%, was an independent risk factor for BP elevation (odds ratio [OR], 1.56; 95% confidence interval [CI], 1.27-1.92); other risk factors included age ≥60 years (OR, 1.26; 95% CI, 1.06-1.52), and body mass index (BMI) ≥25 kg/m(2) (OR, 1.26; 95% CI, 1.04-1.53). Race, sex, anti-VEGF therapy prescribed, and baseline antihypertensive class were not significant risk factors. The absolute observed mean increase in BP was 21 mm Hg (systolic)/15 mm Hg (diastolic), both in patients with and without preexisting hypertension. The development of hypertension predicted improved survival (hazard ratio, 0.76; 95% CI, 0.65-0.89).
CONCLUSIONS: Preexisting hypertension, age, and BMI identify patients at risk for significant anti-VEGF therapy-induced BP elevation. Hypertension appears to be a clinical biomarker of efficacy of anti-VEGF therapies in a broad range of malignancies.

PMCID: PMC4293233 [Available on 2016-01-15]
PMID: 25236375 [PubMed - indexed for MEDLINE]

Heart. 2015 Jan;101(2):132-8.

Variation in resting heart rate over 4 years and the risks of myocardial infarction and death mong older adults.

Floyd JS(1), Sitlani CM(1), Wiggins KL(1), Wallace E(2), Suchy-Dicey A(2), Abbasi SA(3), Carnethon MR(4), Siscovick DS(5), Sotoodehnia N(1), Heckbert SR(6), McKnight B(7), Rice KM(7), Psaty BM(5).

OBJECTIVE: Resting heart rate (RHR) is an established predictor of myocardial infarction (MI) and mortality, but the relationship between variation in RHR over a period of several years and health outcomes is unclear. We evaluated the relationship between long-term variation in RHR and the risks of incident MI and mortality among older adults.
METHODS: 1991 subjects without cardiovascular disease from the Cardiovascular Health Study were included. RHR was taken from resting ECGs at the first five annual study visits. RHR mean, trend and

variation were estimated with linear regression. Subjects were followed for incident MI and death until December 2010. HRs for RHR mean, trend and variation are reported for differences of 10 bpm, 2 bpm/year and 2 bpm, respectively.

RESULTS: 262 subjects had an incident MI event (13%) and 1326 died (67%) during 12 years of median follow-up. In primary analyses adjusted for cardiovascular risk factors, RHR mean (HR 1.12; 95% CI 1.05 to 1.20) and variation (HR 1.08; 95% CI 1.03 to 1.13) were associated with the risk of death while trend was not. None of the RHR variables were significantly associated with the risk of incident MI events; however, CIs were wide and the MI associations with RHR variables were not significantly different from the mortality associations. Adjusting for additional variables did not affect estimates, and there were no significant interactions with sex.

CONCLUSIONS: Variation in RHR over a period of several years represents a potential predictor of long-term mortality among older persons free of cardiovascular disease.

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Heart. 2015 Jan;101(1):44-9.

Metabolic syndrome is associated with and predicted by resting heart rate: a cross-sectional and longitudinal study.

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OBJECTIVE: Although higher resting heart rate (RHR) has emerged as a predictor for lifespan, the underlying mechanisms remain obscure. The present study investigates whether a positive relationship exists between RHR and metabolic syndrome (MetS) and whether RHR predicts future MetS.

METHODS: A cohort of 89,860 participants were surveyed during 2006-2007 in Kailuan/Tangshan, China. MetS was diagnosed when a participant presented at least three of the following: abdominal adiposity, low high density lipoprotein-cholesterol, high triglycerides, hypertension or impaired fasting glucose. RHR was derived from ECG recordings and subjects were stratified based on RHR. Some participants without MetS at baseline were followed-up for 4 years.

RESULTS: At baseline, 23,150 participants (25.76%) had MetS. There was a positive association between RHR and MetS. The OR of having MetS was 1.49 (95% CI 1.32 to 1.69) in subjects with RHR at 95-104 compared with those at 55-64 beats per minute (bpm) (reference), after adjusting for variables including age, sex, education, cigarette smoking, alcohol drinking, physical activities, body mass index, hypertension, diabetes, hyperlipidaemia, inflammatory biomarkers and renal function. More importantly, when 43,725 individuals from the original study without MetS at baseline were

followed-up, higher RHR was found to predict greater risk of MetS incidence. The OR of developing MetS 4 years later was 1.41 (95% CI 1.21 to 1.65) in subjects with RHR at 95-104 bpm compared with reference, after all adjustments.
CONCLUSIONS: Our cross-sectional and longitudinal findings provide evidence that RHR is an independent risk factor for existing MetS and a powerful predictor for future incidence of MetS.

PMID: 25179964 [PubMed - indexed for MEDLINE]

Chest. 2015 Jan;147(1):150-6.

Risk factors for cardiovascular disease in people with idiopathic pulmonary fibrosis: a opulation-based study.

Dalleywater W, Powell HA, Hubbard RB, Navaratnam V.

OBJECTIVE: People with idiopathic pulmonary fibrosis (IPF) have been shown to be at an increased risk for cardiovascular (CV) disease, but reasons for this are unknown. The aim of this study was to compare the prevalence of common CV risk factors in people with IPF and the general population and establish the incidence of ischemic heart disease (IHD) and stroke after the diagnosis of IPF, controlling for these risk factors.
METHODS: We used data from a large, UK primary care database to identify incident cases of IPF and matched general-population control subjects. We compared the prevalence of risk factors for CV disease and prescription of CV medications in people with IPF (before diagnosis) with control subjects from the general population and assessed the incidence of IHD and stroke in people with IPF (after diagnosis) compared with control subjects.
RESULTS: We identified 3,211 cases of IPF and 12,307 control subjects. Patients with IPF were more likely to have a record of hypertension (OR, 1.31; 95% CI, 1.19-1.44), and diabetes (OR, 1.20; 95% CI, 1.07-1.34) compared with control subjects; they were also more likely to have been prescribed several CV drugs. The rate of first-time IHD events was more than twice as high in patients than control subjects (rate ratio, 2.32; 95% CI, 1.85-2.93; P < .001), but the incidence of stroke was only marginally higher (P = .09). Rate ratios for IHD and stroke were not altered substantially after adjusting for CV risk factors.
CONCLUSIONS: Several CV risk factors were more prevalent in people with IPF; however, this did not account for the increased rate of IHD in this group of patients.

PMID: 25121965 [PubMed - indexed for MEDLINE]

Heart. 2015 Jan;101(1):17-22.

Sudden cardiac death is associated both with epilepsy and with use of antiepileptic medications.

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Comment in
Heart. 2015 Jan;101(1):83.

OBJECTIVE: Epilepsy is associated with increased risk for sudden cardiac death (SCD). We aimed to establish, in a community based study, whether this association is mediated by epilepsy per se, use of antiepileptic medications (AEMs), or both.
METHODS: We studied SCD cases and age/sex matched controls in a case-control study in a large scale general practitioners' research database (n=478 661patients). SCD risk for symptomatic epilepsy (seizure <2 years before SCD), stable epilepsy (no seizure <2 years before SCD), and use of AEMs (any indication) was determined.
RESULTS: We identified 926 SCD cases and 9832 controls. Fourteen cases had epilepsy. Epilepsy was associated with an increased SCD risk (cases 1.5%, controls 0.5%; adjusted OR 2.8, 95% CI 1.4 to 5.3). SCD risk was increased for symptomatic epilepsy (cases 0.9%, controls 0.1%; adjusted OR 5.8, 95% CI 2.1 to 15.6), but not with stable epilepsy (cases 0.6%, controls 0.4%; adjusted OR 1.6, 95% CI 0.7 to 4.1). AEM use was found in 23 cases and was associated with an increased SCD risk (cases 2.5%, controls 0.8%; adjusted OR overall 2.6, 95% CI 1.5 to 4.3) among symptomatic epilepsy cases (cases 0.9%, controls 0.1%; adjusted OR 6.4, 95% CI 2.4 to 17.4) and non-epilepsy cases (cases 1.0%, controls 0.4%; adjusted OR 2.3, 95% CI 1.01 to 5.2). Increased SCD risk was associated with sodium channel blocking AEMs (cases 1.6%, controls 0.4%; adjusted OR 2.8, 95% CI 1.1 to 7.2), but not with non-sodium channel blocking AEMs. Carbamazepine and gabapentin were associated with increased SCD risk (carbamazepine: cases 1.1%, controls 0.3%; adjusted OR 3.2, 95% CI 1.1 to 9.2; gabapentin: cases 0.3%, controls 0.1%; adjusted OR 5.7, 95% CI 1.2 to 27.9).
CONCLUSIONS: Epilepsy and AEM use are both associated with increased SCD risk in the general population. Poor seizure control contributes to increased SCD risk in epilepsy, while sodium channel blockade contributes to SCD susceptibility in AEM users.

PMID: 25031263 [PubMed - indexed for MEDLINE]

Diabetes. 2015 Jan;64(1):257-65..

Plasma advanced glycation end products are associated with incident cardiovascular events in individuals with type 2 diabetes: a case-cohort study with a median follow-up of 10 years (EPIC-NL).

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Comment in

Diabetes. 2015 Jan;64(1):9-11.

Experimental data suggest a role for advanced glycation end products (AGEs) in cardiovascular disease (CVD), particularly in type 2 diabetes (T2DM). However, epidemiological evidence of an association between high plasma AGEs and increased cardiovascular risk remains inconclusive. Therefore, in a case-cohort study comprising 134 cardiovascular case subjects and a random subcohort of 218 individuals (including 65 cardiovascular case subjects), all with T2DM and nested in the European Prospective Investigation into Cancer and Nutrition in the Netherlands (EPIC-NL) study, plasma levels of protein-bound Nε-(carboxymethyl)lysine, Nε-(carboxyethyl)lysine, and pentosidine were measured with liquid chromatography. AGEs were loge-transformed, combined in a z-score, and the association with incident cardiovascular events was analyzed with Cox proportional hazard regression, adapted for case-cohort design (Prentice method). After multivariable adjustment (sex, age, cohort status, diabetes duration, total cholesterol to HDL-cholesterol ratio, smoking, systolic blood pressure, BMI, blood pressure-, cholesterol- and glucose-lowering treatment, prior cardiovascular events, and triglycerides), higher plasma AGE z-scores were associated with higher risk of incident cardiovascular events in individuals without prior cardiovascular events (hazard ratio 1.31 [95% CI: 1.06-1.61]). A similar trend was observed in individuals with prior cardiovascular events (1.37 [0.63-2.98]). In conclusion, high plasma AGEs were associated with incident cardiovascular events in individuals with T2DM. These results underline the potential importance of AGEs in development of CVD.

PMID: 24848072 [PubMed - indexed for MEDLINE]

Am Heart J. 2015 Mar;169(3):356-62.

The impact of smoking on long-term outcome of patients with premature (≤35years) ST-segment elevation acute myocardial infarction.

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BACKGROUND: There are few data regarding the long-term prognosis of young survivors of acute myocardial infarction (AMI). We explored the long-term outcome in individuals who had sustained a premature ST-segment elevation AMI. METHODS: We recruited 257 consecutive patients who had survived their first AMI ≤35years of age. Patients were followed up for up to 18years. Clinical end

points included all major adverse coronary events (MACE): cardiac death, readmission for acute coronary syndrome, arrhythmias, or coronary revascularization due to clinical deterioration.
RESULTS: The most prevalent risk factor at presentation was smoking (93.7%). Follow-up data were obtained from 237 patients (32.2±3.7years old). The median follow-up period was 9.1years. During follow-up, 139 (58.6%) patients reported continuation of smoking. Ninety-one (38.4%) patients had recurrent MACE (13 deaths, 59 acute coronary syndromes, 2 arrhythmias, and 17 revascularizations). Multivariable Cox regression analysis showed that persistence of smoking, left ventricular ejection fraction (LVEF), and reperfusion therapy (fibrinolysis or primary coronary angioplasty) were independent predictors of MACE after adjustment for conventional risk factors. Continuation of smoking remained an independent predictor for MACE after additional adjustments for LVEF (hazard ratio 2.154, 95% CI 1.313-3.535, P=.002) or reperfusion treatment (hazard ratio 2.327, 95% CI 1.423-3.804, P=.001). Harrell c statistic showed that the model with persistent smoking had the best discriminatory power compared with models with LVEF or reperfusion treatment.
CONCLUSIONS: In the era of statins and reperfusion treatment, continuation of smoking is the strongest independent long-term predictor for recurrent MACE in young survivors of premature AMI.

PMID: 25728725 [PubMed - indexed for MEDLINE]

JAMA. 2015 Feb 24;313(8):805-14.

Association of NSAID use with risk of bleeding and cardiovascular events in patients receiving antithrombotic therapy after myocardial infarction.

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Comment in
JAMA. 2015 Feb 24;313(8):801-2.

IMPORTANCE: Antithrombotic treatment is indicated for use in patients after myocardial infarction (MI); however, concomitant use of nonsteroidal anti-inflammatory drugs (NSAIDs) could pose safety concerns.
OBJECTIVE: To examine the risk of bleeding and cardiovascular events among patients with prior MI taking antithrombotic drugs and for whom NSAID therapy was then prescribed.
DESIGN, SETTING, AND PARTICIPANTS: Using nationwide administrative registries in Denmark (2002-2011), we studied patients 30 years or older admitted with first-time MI and alive 30 days after discharge. Subsequent treatment with aspirin, clopidogrel, or oral anticoagulants and their combinations, as well as ongoing concomitant NSAID use, was determined.
EXPOSURES: Use of NSAIDs with ongoing antithrombotic treatment after first-time MI.

MAIN OUTCOMES AND MEASURES: Risk of bleeding (requiring hospitalization) or a composite cardiovascular outcome (cardiovascular death, nonfatal recurrent MI, and stroke) according to ongoing NSAID and antithrombotic therapy, calculated using adjusted time-dependent Cox regression models.
RESULTS: We included 61,971 patients (mean age, 67.7 [SD, 13.6] years; 63% men); of these, 34% filled at least 1 NSAID prescription. The number of deaths during a median follow-up of 3.5 years was 18,105 (29.2%). A total of 5288 bleeding events (8.5%) and 18,568 cardiovascular events (30.0%) occurred. The crude incidence rates of bleeding (events per 100 person-years) were 4.2 (95% CI, 3.8-4.6) with concomitant NSAID treatment and 2.2 (95% CI, 2.1-2.3) without NSAID treatment, whereas the rates of cardiovascular events were 11.2 (95% CI, 10.5-11.9) and 8.3 (95% CI, 8.2-8.4). The multivariate-adjusted Cox regression analysis found increased risk of bleeding with NSAID treatment compared with no NSAID treatment (hazard ratio, 2.02 [95% CI, 1.81-2.26]), and the cardiovascular risk was also increased (hazard ratio, 1.40 [95% CI, 1.30-1.49]). An increased risk of bleeding and cardiovascular events was evident with concomitant use of NSAIDs, regardless of antithrombotic treatment, types of NSAIDs, or duration of use.
CONCLUSIONS AND RELEVANCE: Among patients receiving antithrombotic therapy after MI, the use of NSAIDs was associated with increased risk of bleeding and excess thrombotic events, even after short-term treatment. More research is needed to confirm these findings; however, physicians should exercise appropriate caution when prescribing NSAIDs for patients who have recently experienced MI.

PMID: 25710657 [PubMed - indexed for MEDLINE]

Med Clin North Am. 2015 Mar;99(2):379-89.

Hypertension in the geriatric population: a patient-centered approach.

Kithas PA(1), Supiano MA(2).

Hypertension contributes greatly to adverse cardiovascular outcomes; the magnitude of this contribution increases with age. The most recent guideline has proposed raising the goal systolic blood pressure to less than 150 mm Hg among those over age 60; however, this recommendation is not endorsed by other organizations. There are multiple contributors to hypertension in the older individual, including increased vascular stiffness, salt sensitivity, and decreased baroreceptor responsiveness. Therapy in the hypertensive patient over age 60 should be individualized and account for patient's health, functional and cognitive status, comorbidities, frailty, and prognosis.

PMID: 25700589 [PubMed - indexed for MEDLINE]

J Am Coll Cardiol. 2015 Feb 17;65(6):521-9.

Ischemic brain lesions after carotid artery stenting increase future cerebrovascular risk.

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Comment in

J Am Coll Cardiol. 2015 Feb 17;65(6):530-2.

BACKGROUND: Brain lesions on diffusion-weighted imaging (DWI) are frequently found after carotid artery stenting (CAS), but their clinical relevance remains unclear.

OBJECTIVES: This study sought to investigate whether periprocedural ischemic DWI lesions after CAS or carotid endarterectomy (CEA) are associated with an increased risk of recurrent cerebrovascular events.

METHODS: In the magnetic resonance imaging (MRI) substudy of ICSS (International Carotid Stenting Study), 231 patients with symptomatic carotid stenosis were randomized to undergo CAS (n=124) or CEA (n=107). MRIs were performed 1 to 7 days before and 1 to 3 days after treatment. The primary outcome event was stroke or transient ischemic attack in any territory occurring between the post-treatment MRI and the end of follow-up. Time to occurrence of the primary outcome event was compared between patients with (DWI+) and without (DWI-) new DWI lesions on the post-treatment scan in the CAS and CEA groups separately.

RESULTS: Median time of follow-up was 4.1 years (interquartile range: 3.0 to5.2). In the CAS group, recurrent stroke or transient ischemic attack occurred more often among DWI+ patients (12 of 62) than among DWI- patients (6 of 62), with a cumulative 5-year incidence of 22.8% (standard error [SE]: 7.1%) and 8.8% (SE: 3.8%), respectively (unadjusted hazard ratio: 2.85; 95% confidence interval: 1.05 to 7.72; p=0.04). In DWI+ and DWI- patients, 8 and 2 events, respectively, occurred within 6 months after treatment. In the CEA group, there was no difference in recurrent cerebrovascular events between DWI+ and DWI- patients.

CONCLUSIONS: Ischemic brain lesions discovered on DWI after CAS seem to be a marker of increased risk for recurrent cerebrovascular events. Patients with periprocedural DWI lesions might benefit from more aggressive and prolonged antiplatelet therapy after CAS. (A Randomised Comparison of the Risks, Benefits and Cost Effectiveness of Primary Carotid Stenting With Carotid Endarterectomy: International Carotid Stenting Study; ISRCTN25337470).

PMCID: PMC4323145

PMID: 25677309 [PubMed - indexed for MEDLINE]

Medicine (Baltimore). 2015 Feb;94(5):e485.

Higher physical activity is associated with lower aortic stiffness but not with central blood pressure: the ADDITION-Pro Study.

Laursen AS(1), Hansen AL, Wiinberg N, Brage S, Sandbæk A, Lauritzen T, Witte DR, Jørgensen ME, Johansen NB.

Physical activity is associated with reduced cardiovascular disease risk. However, improvements in conventional risk factors due to physical activity do not explain its full benefit. Therefore, we examined associations of objectively measured physical activity energy expenditure and intensity with central hemodynamics to provide new insight into the link between physical activity and cardiovascular disease. We analyzed data from 1816 Danes (median age: 66 years) without cardiovascular disease. Physical activity was estimated using combined accelerometry and heart rate monitoring. Aortic stiffness was assessed by applanation tonometry, as aortic pulse wave velocity, and central blood pressure was estimated from radial waveforms. Associations between physical activity energy expenditure and central hemodynamics were examined by linear regression. Furthermore, the consequence of substituting 1hour sedentary behavior with 1hour light or moderate-to-vigorous physical activity on central hemodynamics was examined. Median physical activity energy expenditure was 28.0kJ/kg/d (IQR: 19.8; 38.7). A 10kJ/kg/d higher energy expenditure was associated with 0.75% lower aortic pulse wave velocity (CI: -1.47; -0.03). Associations with central systolic blood pressure and central pulse pressure were not statistically significant. We observed no difference in central hemodynamics when substituting 1hour sedentary behavior with 1hour light or moderate-to-vigorous physical activity. In this relatively inactive population, higher physical activity energy expenditure was associated with lower aortic stiffness, while there was no statistically significant association between substitution of activity intensity and central hemodynamics. This suggests that lower aortic stiffness is one of a number of health benefits attributed to higher habitual physical activity.

PMID: 25654392 [PubMed - indexed for MEDLINE]

Mayo Clin Proc. 2015 Mar;90(3):339-45.

Effect of physical activity assessment on prognostication for peripheral artery disease and mortality.

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OBJECTIVE: To examine whether a simple question about the performance of regular vigorous activity is associated with peripheral artery disease (PAD) and mortality.

METHODS: A total of 1288 individuals undergoing nonemergency coronary angiography were assessed for participation in regular vigorous activity by questionnaire. Data on demographic characteristics, ankle-brachial indexes, and cardiovascular outcomes were prospectively collected.
RESULTS: Compared with those who denied participation in regular vigorous activity, those who reported participation were less likely to have PAD (odds ratio, 0.58; 95% CI, 0.39-0.86), had higher ankle-brachial indexes, had better Walking Impairment Questionnaire scores (P<.001), and experienced reduced all-cause mortality rates (hazard ratio, 0.48; 95% CI, 0.31-0.74). When added to the Framingham Risk Score, the response improved the net reclassification index for all-cause (32.6%) and cardiovascular (32.0%) mortality.
CONCLUSION: Among at-risk individuals, regular vigorous activity is associated with decreased PAD and all-cause mortality. Simple and readily available, a single yes/no query about participation in regular vigorous exercise could be used to improve risk stratification.

PMID: 25649965 [PubMed - indexed for MEDLINE]

Neurology. 2015 Feb 24;84(8):833-40.

Subclinical cardiac dysfunction increases the risk of stroke and dementia: the Rotterdam Study.

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OBJECTIVE: To investigate the association between cardiac function and the risk of stroke and dementia in elderly free of clinical cardiac disease. Additionally, we investigated the relation between cardiac function and MRI markers of subclinical cerebrovascular disease.
METHODS: This study was conducted within the population-based Rotterdam Study. A total of 3,291 participants (60.8% female, age-range 58-98 years) free of coronary heart disease, heart failure, atrial fibrillation, stroke, and dementia underwent echocardiography in 2002-2005 to measure cardiac function. Follow-up finished in 2012. In 2005-2006, a random subset of 577 stroke-free people without dementia underwent brain MRI on which infarcts and white matter lesion volume were assessed.
RESULTS: During 21,785 person-years of follow-up, 164 people had a stroke and during 19,462 person-years of follow-up, 208 people developed dementia. Measures of better diastolic function, such as higher E/A ratio, were associated with a lower risk of stroke (hazard ratio [HR] 0.82; 95% confidence interval [CI] 0.69; 0.98) and dementia (HR 0.82; 95% CI 0.70; 0.96). Better systolic function, measured as higher fractional shortening, was only associated with a lower risk of stroke (HR 0.84; 95% CI 0.72; 0.98). Better diastolic function was related to a lower prevalence of silent infarcts on MRI, especially lacunar infarcts.
CONCLUSIONS: In elderly free of clinical cardiac disease, worse diastolic function is associated with clinical stroke, dementia, and silent infarcts on MRI, whereas worse systolic function is related only to

clinical stroke. These findings can form the basis for future research on the utility of cardiac function as potential intervention target for prevention of neurologic diseases.

PMID: 25632093 [PubMed - indexed for MEDLINE]

JAMA. 2015 Jan 20;313(3):264-74.

Association between hospitalization for pneumonia and subsequent risk of cardiovascular disease.

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IMPORTANCE: The risk of cardiovascular disease (CVD) after infection is poorly understood.
OBJECTIVE: To determine whether hospitalization for pneumonia is associated with an increased short-term and long-term risk of CVD.
DESIGN, SETTINGS, AND PARTICIPANTS: We examined 2 community-based cohorts: the Cardiovascular Health Study (CHS, n=5888; enrollment age, ≥65 years; enrollment period, 1989-1994) and the Atherosclerosis Risk in Communities study (ARIC, n=15,792; enrollment age, 45-64 years; enrollment period, 1987-1989). Participants were followed up through December 31, 2010. We matched each participant hospitalized with pneumonia to 2 controls. Pneumonia cases and controls were followed for occurrence of CVD over 10 years after matching. We estimated hazard ratios (HRs) for CVD at different time intervals, adjusting for demographics, CVD risk factors, subclinical CVD, comorbidities, and functional status.
EXPOSURES: Hospitalization for pneumonia.
MAIN OUTCOMES AND MEASURES: Incident CVD (myocardial infarction, stroke, and fatal coronary heart disease).
RESULTS: Of 591 pneumonia cases in CHS, 206 had CVD events over 10 years after pneumonia hospitalization. CVD risk after pneumonia was highest in the first year. CVD occurred in 54 cases and 6 controls in the first 30 days (HR, 4.07; 95% CI, 2.86-5.27); 11 cases and 9 controls between 31 and 90 days (HR, 2.94; 95% CI, 2.18-3.70); and 22 cases and 55 controls between 91 days and 1 year (HR, 2.10; 95% CI, 1.59-2.60). Additional CVD risk remained elevated into the tenth year, when 4 cases and 12 controls developed CVD (HR, 1.86; 95% CI, 1.18-2.55). In ARIC, of 680 pneumonia cases, 112 had CVD over 10 years after hospitalization. CVD occurred in 4 cases and 3 controls in the first 30 days (HR, 2.38; 95% CI, 1.12-3.63); 4 cases and 0 controls between 31 and 90 days (HR, 2.40; 95% CI, 1.23-3.47); 11 cases and 8 controls between 91 days and 1 year (HR, 2.19; 95% CI, 1.20-3.19); and 8 cases and 7 controls during the second year (HR, 1.88; 95% CI, 1.10-2.66). After the second year, the HRs were no longer statistically significant.

CONCLUSIONS AND RELEVANCE: Hospitalization for pneumonia was associated with increased short-term and long-term risk of CVD, suggesting that pneumonia may be a risk factor for CVD.

PMID: 25602997 [PubMed - indexed for MEDLINE]

Ann Intern Med. 2015 Jan 20;162(2):123-32.

Sedentary time and its association with risk for disease incidence, mortality, and hospitalization in adults: a systematic review and meta-analysis.

Biswas A, Oh PI, Faulkner GE, Bajaj RR, Silver MA, Mitchell MS, Alter DA.

Comment in
BMJ. 2015;350:h306.
Ann Intern Med. 2015 Jan 20;162(2):146-7.

BACKGROUND: The magnitude, consistency, and manner of association between sedentary time and outcomes independent of physical activity remain unclear.
PURPOSE: To quantify the association between sedentary time and hospitalizations, all-cause mortality, cardiovascular disease, diabetes, and cancer in adults independent of physical activity.
DATA SOURCES: English-language studies in MEDLINE, PubMed, EMBASE, CINAHL, Cochrane Library, Web of Knowledge, and Google Scholar databases were searched through August 2014 with hand-searching of in-text citations and no publication date limitations.
STUDY SELECTION: Studies assessing sedentary behavior in adults, adjusted for physical activity and correlated to at least 1 outcome.
DATA EXTRACTION: Two independent reviewers performed data abstraction and quality assessment, and a third reviewer resolved inconsistencies.
DATA SYNTHESIS: Forty-seven articles met our eligibility criteria. Meta-analyses were performed on outcomes for cardiovascular disease and diabetes (14 studies), cancer (14 studies), and all-cause mortality (13 studies). Prospective cohort designs were used in all but 3 studies; sedentary times were quantified using self-report in all but 1 study. Significant hazard ratio (HR) associations were found with all-cause mortality (HR, 1.240 [95% CI, 1.090 to 1.410]), cardiovascular disease mortality (HR, 1.179 [CI, 1.106 to 1.257]), cardiovascular disease incidence (HR, 1.143 [CI, 1.002 to 1.729]), cancer mortality (HR, 1.173 [CI, 1.108 to 1.242]), cancer incidence (HR, 1.130 [CI, 1.053 to 1.213]), and type 2 diabetes incidence (HR, 1.910 [CI, 1.642 to 2.222]). Hazard ratios associated with sedentary time and outcomes were generally more pronounced at lower levels of physical activity than at higher levels.
LIMITATION: There was marked heterogeneity in research designs and the assessment of sedentary time and physical activity.

CONCLUSION: Prolonged sedentary time was independently associated with deleterious health outcomes regardless of physical activity.
PRIMARY FUNDING SOURCE: None.

PMID: 25599350 [PubMed - indexed for MEDLINE]

Am J Cardiol. 2015 Feb 15;115(4):411-6

Relation between paradoxical decrease in high-density lipoprotein cholesterol levels after statin therapy and adverse cardiovascular events in patients with acute myocardial infarction.

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Statin therapy moderately increases high-density lipoprotein cholesterol (HDL-C) levels. Contrary to this expectation, a paradoxical decrease in HDL-C levels after statin therapy is seen in some patients. We evaluated 724 patients who newly started treatment with statins after acute myocardial infarction (AMI). These patients were divided into 2 groups according to change in HDL-C levels between baseline and 6 to 9 months after initial AMI (ΔHDL). In total, 620 patients had increased HDL-C levels and 104 patients had decreased HDL-C levels. Both groups achieved follow-up low-density lipoprotein cholesterol levels <100 mg/dl. Adverse cardiovascular events (a composite of all-cause death, myocardial infarction, and stroke) have more frequently occurred in the decreased HDL group compared with the increased HDL group (15.4% vs 7.1%, p = 0.01). Multivariate analysis showed that decreased HDL, onset to balloon time, and multivessel disease were the independent predictors of adverse cardiovascular events (hazard ratio [HR] 1.95, 95% confidence interval [CI] 1.08 to 3.52; HR 1.05, 95% CI 1.01 to 1.09; and HR 2.08, 95% CI 1.22 to 3.56, respectively). In conclusion, a paradoxical decrease in serum HDL-C levels after statin therapy might be an independent predictor of long-term adverse cardiovascular events in patients with AMI.

PMID: 25555656 [PubMed - indexed for MEDLINE]

Am J Cardiol. 2015 Feb 15;115(4):441-6.

Effect of statin therapy on incident type 2 diabetes mellitus in patients with clinically manifest vascular disease.

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Several trials and cohort studies have shown an increased incidence of type 2 diabetes mellitus (T2DM) in patients using statins. Whether this only applies to patients at already high risk for the development of T2DM or for all patients is still a matter of debate. In the present prospective cohort study of 4,645 patients with established vascular disease without DM at baseline, 3,057 patients used statins at baseline, of whom 1,608 used intensive statin therapy, defined as statin therapy theoretically lowering low-density lipoprotein cholesterol with ≥40%. Cox proportional hazards models were used to estimate the risk of incident T2DM with (intensive) statin therapy. Statin therapy was associated with increased risk of incident T2DM (hazard ratio 1.63; 95% confidence interval 1.15 to 2.32) when adjusted for age, gender, body mass index, plasma high-density lipoprotein cholesterol, and plasma triglyceride levels. Intensive statin therapy tended to be related to a higher risk of T2DM compared with moderate statin therapy (hazard ratio 1.22; 95% confidence interval 0.92 to 1.61, adjusted for age, gender, body mass index, plasma high-density lipoprotein cholesterol, and plasma triglyceride levels). The increase in risk was regardless of the number of metabolic syndrome characteristics or insulin resistance but was particularly present in patients with low baseline glucose levels (<5.6 mmol/L; p for interaction 2.9 × 10(-7)). In conclusion, statin use increases the risk of incident T2DM in patients with clinically manifest vascular disease. The increase in risk was independent of the number of metabolic syndrome criteria and was even more pronounced in patients with low baseline glucose levels.

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Insulin resistance in rheumatoid arthritis: disease-related indicators and associations with the presence and progression of subclinical atherosclerosis.

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OBJECTIVE: Systemic inflammation and insulin resistance (IR) are linked, yet the determinants of IR and its impact on atherosclerosis in rheumatoid arthritis (RA) are incompletely understood. The aim of this study was to explore the prevalence of IR in RA and non-RA populations and investigate whether the associations of IR with measures of atherosclerosis differ between these groups.
METHODS: IR was quantified using the homeostatic model assessment of IR (HOMA-IR), and was compared between RA patients and demographically matched non-RA controls. Differences in the

associations between the HOMA-IR index and the Agatston coronary artery calcium (CAC) score, ultrasound-determined intima-media thickness (IMT) of the common carotid artery (CCA) and internal carotid artery (ICA), and focal plaque in the ICA/carotid bulb were compared according to RA status.
RESULTS: Among the 195 RA patients and 198 controls studied, average HOMA-IR levels were higher in the RA group by 31%, and were consistently higher in the RA group regardless of stratification by demographic or cardiometabolic risk factors. While the HOMA-IR index was strongly and significantly associated with C-reactive protein (CRP) and interleukin-6 (IL-6) levels in the control group, the association was weaker in the RA group. Among RA patients, higher HOMA-IR levels were associated with rheumatoid factor (RF) seropositivity in men and women, and prednisone use in women only. Before adjustment, higher HOMA-IR levels were associated with all assessed measures of subclinical atherosclerosis in the control group only; associations were diminished and lost statistical significance after adjustment for cardiovascular risk factors. Among the RA patients, neither baseline nor average HOMA-IR levels were significantly associated with change in any of the atherosclerosis measures over an average of 3.2 years of followup.
CONCLUSION: Although IR was higher in RA patients than in non-RA controls, higher levels may not independently impart additional risk of atherosclerosis.

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Relation of metabolic syndrome with long-term mortality in acute and stable coronary disease.

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Past studies examining the effects of the metabolic syndrome (MS) on prognosis in postangiography patients were limited in size or were controversial in results. The aim of the study was to examine the association of the MS and the risk for long-term mortality in a large cohort of patients undergoing coronary angiography for various clinical indications. Medical history, physical examination, and laboratory values were used to diagnose patients with the MS. Cox regression models were used to analyze the effect of MS on long-term all-cause mortality. We prospectively recruited 3,525 consecutive patients with a mean age of 66 ± 22 years (range 24 to 97) and 72% men. Thirty percent of the cohort had MS. Patients with MS were more likely to have advanced coronary artery disease and acute coronary syndrome ($p < 0.001$). Patients with MS had more abnormalities in their metabolic and inflammatory biomarkers regardless of their clinical presentation. A total of 495 deaths occurred during a mean follow-up period of 1,614 ± 709 days (median 1,780, interquartile range 1,030 to 2,178). MS was associated with an increased risk of death in the general cohort (hazard ratio [HR] 1.27, 95% confidence interval [CI] 1.01 to 1.56, $p = 0.02$). MS had a significant effect on mortality in

stable patients (HR 1.55, 95% CI 1.1 to 2.18, p = 0.01), whereas it did not have a significant effect on mortality in patients with acute coronary syndrome (HR 1.11, 95% CI 0.86 to 1.44, p = 0.42). In conclusion, MS is associated with increased mortality in postangiography patients. Its adverse outcome is mainly seen in patients with stable angina.

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Effect of psoriasis severity on hypertension control: a population-based study in the United Kingdom.

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IMPORTANCE: Hypertension is prevalent among patients with psoriasis. The effect of psoriasis and its severity on hypertension control is unknown.
OBJECTIVE: To determine the association between uncontrolled blood pressure and psoriasis, both overall and according to objectively measured psoriasis severity, among patients with diagnosed hypertension.
DESIGN, SETTING, AND PARTICIPANTS: Population-based cross-sectional study nested in a prospective cohort drawn from The Health Improvement Network (THIN), an electronic medical records database broadly representative of the general population in the United Kingdom. The study population included a random sample of patients with psoriasis (n = 1322) between the ages of 25 and 64 years in THIN who were included in the Incident Health Outcomes and Psoriasis Events prospective cohort and their age- and practice-matched controls without psoriasis (n = 11,977). All included patients had a diagnosis of hypertension; their psoriasis diagnosis was confirmed and disease severity was classified by their general practitioners.
MAIN OUTCOMES AND MEASURES: Uncontrolled hypertension was defined as a systolic blood pressure of 140 mm Hg or higher or a diastolic blood pressure of 90 mm Hg or higher based on the blood pressure recorded closest in time to the assessment of psoriasis severity.
RESULTS: There was a significant positive dose-response relationship between uncontrolled hypertension and psoriasis severity as objectively determined by the affected body surface area in both unadjusted and adjusted analyses that controlled for age, sex, body mass index, smoking and alcohol use status, presence of comorbid conditions, and current use of antihypertensive medications and nonsteroidal anti-inflammatory drugs (adjusted odds ratio [aOR], 0.97; 95% CI, 0.82-1.14 for mild psoriasis; aOR, 1.20; 95% CI, 0.99-1.45 for moderate psoriasis; and aOR, 1.48; 95% CI, 1.08-2.04 for severe psoriasis; P = .01 for trend). The likelihood of uncontrolled hypertension among psoriasis overall was also increased, although not statistically significantly so (aOR, 1.10; 95% CI, 0.98-1.24).

CONCLUSIONS AND RELEVANCE: Among patients with hypertension, psoriasis was associated with a greater likelihood of uncontrolled hypertension in a dose-dependent manner, with the greatest likelihood observed among those with moderate to severe psoriasis defined by 3% or more of the body surface area affected. Our data suggest a need for more effective blood pressure management, particularly among patients with more severe psoriasis.

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A cardiovascular disease policy model that predicts life expectancy taking into account socioeconomic deprivation.

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OBJECTIVES: A policy model is a model that can evaluate the effectiveness and cost-effectiveness of interventions and inform policy decisions. In this study, we introduce a cardiovascular disease (CVD) policy model which can be used to model remaining life expectancy including a measure of socioeconomic deprivation as an independent risk factor for CVD.
DESIGN: A state transition model was developed using the Scottish Heart Health Extended Cohort (SHHEC) linked to Scottish morbidity and death records. Individuals start in a CVD-free state and can transit to three CVD event states plus a non-CVD death state. Individuals who have a non-fatal first event are then followed up until death. Taking a competing risk approach, the cause-specific hazards of a first event are modelled using parametric survival analysis. Survival following a first non-fatal event is also modelled parametrically. We assessed discrimination, validation and calibration of our model.
RESULTS: Our model achieved a good level of discrimination in each component (c-statistics for men (women)-non-fatal coronary heart disease (CHD): 0.70 (0.74), non-fatal cerebrovascular disease (CBVD): 0.73 (0.76), fatal CVD: 0.77 (0.80), fatal non-CVD: 0.74 (0.72), survival after non-fatal CHD: 0.68 (0.67) and survival after non-fatal CBVD: 0.65 (0.66)). In general, our model predictions were comparable with observed event rates for a Scottish randomised statin trial population which has an overlapping follow-up period with SHHEC. After applying a calibration factor, our predictions of life expectancy closely match those published in recent national life tables.
CONCLUSIONS: Our model can be used to estimate the impact of primary prevention interventions on life expectancy and can assess the impact of interventions on inequalities.

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