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Índice

BMC Endocr Disord. 2017 Mar 9;17(1):15. doi: 10.1186/s12902-017-0166-6.

The association between biochemical control and cardiovascular risk factors in acromegaly.

Carmichael JD, Broder MS, Cherepanov D, Chang E, Mamelak A, Said Q, Neary MP, Bonert V.

BACKGROUND: The study aim was to estimate the proportion of acromegaly patients with various comorbidities and to determine if biochemical control was associated with reduced proportion of cardiovascular risk factors.

METHODS: Data were from a single-center acromegaly registry. Study patients were followed for ≥12 months after initial treatment. Study period was from first to last insulin-like growth factor-I and growth hormone tests.

RESULTS: Of 121 patients, 55% were female. Mean age at diagnosis was 42.4 (SD: 15.0). Mean study period was 8.8 (SD: 7.2) years. Macroadenomas were observed in 93 of 106 patients (87.7%), and microadenomas in 13 (12.3%). Initial treatment was surgery in 104 patients (86%), pharmacotherapy in 16 (13.2%), and radiation therapy in 1 (0.8%). Of 120 patients, 79 (65.8%) achieved control during the study period. New onset comorbidities (reported 6 months after study start) were uncommon (<10%). Comorbidities were typically more prevalent in uncontrolled versus controlled patients-24 (58.5%) vs. 33 (41.8%) had hypertension, 17 (41.5%) vs. 20 (25.3%) had diabetes, 11 (26.8%) vs. 16 (20.3%) had sleep apnea, and 3 (7.3%) vs. 3 (3.8%) had cardiomyopathy-except for colon polyps or cancer (19.5% vs. 20.3%), left ventricular hypertrophy (9.8% vs. 11.4%), and visual defects (14.6% vs. 17.7%).

CONCLUSIONS: A greater number of comorbidities were observed in biochemically uncontrolled patients with acromegaly compared to their controlled counterparts in this single-center registry. About a third of the patients remained uncontrolled after a mean of >8 years of treatment, demonstrating the difficulty of achieving control in some patients.

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PMID: 28279153 [Indexed for MEDLINE]

BMC Res Notes. 2017 Mar 7;10(1):120.

Total cardiovascular risk for next 10 years among rural population of Nepal using WHO/ISH risk prediction chart.

Khanal MK, Ahmed MS, Moniruzzaman M, Banik PC, Dhungana RR, Bhandari P, Devkota S, Shayami A.

BACKGROUND: Cardiovascular diseases (CVD) are the leading cause of morbidity and mortality globally. Primary prevention of CVD based on total CVD risk approach using WHO/ISH risk prediction chart would be more effective to stratify population under different risk levels, prioritize and utilize the scarce resources of low and middle-income countries. This study estimated total 10-year CVD risk and determined the proportion of population who need immediate drug therapy among the rural population of Nepal.

METHODS: A community based cross-sectional study conducted among 345 participants aged 40-80 years in rural villages of Lamjung District of Nepal. They were selected randomly from total eighteen wards. Data were collected using WHO STEPS questionnaires. WHO/ISH risk prediction chart for SEAR D was used to estimate total cardiovascular risk. Chi-square and independent t-test were used to test significance at the level of $p < 0.05$ in SPSS version 16.0.

RESULTS: Of the total participants, 55.4% were female. The mean age (standard deviation) of the participants was 53.5 ± 10.1 years. According to WHO/ISH chart proportions of low, moderate and high CVD risk were 86.4%, 9.3%, and 4.3%, respectively. Eleven percent of participants were in need of immediate pharmacotherapy. Age ($p = 0.001$), level of education ($p = 0.01$) and occupation ($p = 0.001$) were significantly associated with elevated CVD risk.

CONCLUSION: A large proportion of Nepalese rural population is at moderate and high CVD risk. Immediate pharmacological interventions are warranted for at least one in every ten individuals along with lifestyle interventions. Both population-wise and high-risk approaches are required to minimize CVD burden in the future.

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PMCID: PMC5341399
PMID: 28270186 [Indexed for MEDLINE]

Dan Med J. 2017 Mar;64(3). pii: B5353.

Trends in population blood pressure and determinant factors for population blood pressure.

Andersen UO

Strategies to reduce the burden of blood pressure attributable diseases require knowledge of secular trend in PBP and its determinants. The issues were investigated in the Copenhagen City Heart Study. The design of CCHS is a repeated measures study. Such designs are uniquely suited to studying changes of an outcome and what risk factors may be associated with that outcome. Repeated measures studies are very well suited for trend analysis by using mixed effect analyses. SBP decreased about 2 mmHg in 25 years. The risk factors age, gender and BMI were found valid as determinant factors for secular trends in SBP. In addition, the following factors were identified: household income and the interactions ''gender*age'' and ''survey*age''.

The interaction ''gender*age'' stated that the difference between SBP in the two genders was great in the young individuals and diminished by age. The interaction ''survey*age'' stated that SBP in the young individuals decreased more with survey than SBP in the older individuals. Thus, the 20 years old subjects in survey 2, 3 and 4 have lower SBP than the 20 years old subjects in preceding surveys. The slopes were less steep in higher ages. In the group of elderly and old subjects the trend is partly explained by treatment bias because more and more subjects leave the untreated group and start treatment.

The factor ''household income'' was significant only in the female population and stated that high-income women had lower SBP and a more beneficial secular trend in SBP than low-income women. Marital status, self-reported physical exercise and alcohol intake were not significant factors. A number of factors, that are interesting in relation to SBP, were not included in the CCHS and therefore not investigated. Among them are salt intake, childhood factors, genetic factors and the DASH diet. A survival study was performed to investigate the mortality rate in relation to SBP changes during the observation period.

A Cox regression analysis was used in this study. The survival study demonstrated that SBP was a significant variable in survival models for all age groups. There was a decrease in mortality rate in young to middle-aged individuals. The mortality rate that is associated with a particular value of SBP did not change. Thus, it was concluded that SBP was as dangerous as it has always been and that the reduction in mortality rate was most pronounced in the age classes that also experienced the greatest reduction in blood pressure. During the observation period the number of treated individuals in the population increased from 6.5% to 18.1%. About 50% of the population was hypertensive (SBP ≥ 140 mmHg or treated with antihypertensive medication). The value of SBPtreated was used as an indicator for hypertension control in the treated population.

Hypertension control is a collection of topics that includes guidelines, available medicine, physicians attitude towards hypertension treatment, systematic control, patient awareness and patient compliance. The analysis of trends in SPB in treated hypertensives showed that SBPtreated decreased 9.2 mmHg in 25 years. The result may be ascribed to improvements in treatment but may also be caused by a change in start-to-treat practice: If hypertensives start treatment at an increasingly lower SBPthreshold then SBPtreated will decrease without improvements in treatment. Therefore the start-to-treat practice was evaluated by SBPthreshold. A change in SBPthreshold was

not observed. Thus, the 9.2 mmHg decrease in SBPtreated may represent improvements in treatment. ''Age'' was a significant factor for SBPtreated. This result demonstrated that elderly and old individuals were treated less successful than young and middle-aged individuals.

Subjects diagnosed with ischemic heart disease constitute a group with a more advantageous slope than subjects with other diagnoses (stroke, IHD in combination with stroke, and hypertension alone). Self-reported physical exercise, gender, alcohol intake, household income and family structure were not significant as variables in the decreasing SBP among treated hypertensives.

Thus, the papers in this thesis described SBP trends in the untreated and in the treated part of a population. Different patient-related factors were identified as determinant factors for trends in the two groups. The determinant factors are the explanatory variables most associated with trends in SBP. The determinant factors were different for the two groups (except for age).

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Nucl Med Rev Cent East Eur. 2017;20(1):3-9.

Prevalence of risk factors and asymptomatic carotid atherosclerosis in diabetic patients screened for silent myocardial ischemia by SPECT myocardial imaging.

Mitevska IP, Baneva N, Bosevski M, Kostovska ES.

BACKGROUND: The aim of the study was to evaluate whether there is any association between myocardial ischemia, common risk factors and carotid artery ultrasound parameters in asymptomatic type 2 diabetic (DMT2) patients.

MATERIAL AND METHODS: 60 asymptomatic DMT2 patients (pts) without known coronary artery disease (CAD) underwent one day rest Dypiridamole stress Tc-99m sestamibi single photon emission computed tomography myocardial perfusion scintigraphy (MPS). We used 17 segment models for perfusion analysis with the assessment of perfusion scores. Patients were studied for age, sex, hypertension, hyperlipidemia, hs-CRP, smoking, obesity and family history of cardiac disease. Color Ultrasound examination of carotid arteries was performed in all patients.

RESULTS: 51 patients (pts) had hypertension, 48 pts had hyperlipidemia, 15 were smokers, 6 pts had BMI > 30 kg/m2 and 26 patients had positive family history for CAD. 18 (31%) patients had myocardial ischemia. Mild ischemia was found in 6 pts, moderate in 7 patients and severe ischemia in 5 patients. Carotid IMT was increased in 34 pts and 15 pts had carotid plaques. Mean c-IMT value in patients with normal MPS results was 0.7 ± 0.1; in moderate ischemia 0.9 ± 0.1 and in pts severe ischemia 1.0 ± 0.2. Multivariate analysis showed obesity, low HDL and increased diastolic blood pressure predictors of increased c-IMT. Increased pulse pressure (PP), age and non-HDL cholesterol were predictors for presence of carotid plaques. Multivariable analysis for prediction of stress induced ischemia showed OR 2.9 (95% CI 2.1-5.1) for male gender, OR 3.1 for systolic blood pressure (95% CI 1.9-3.8) and OR 2.8 for LDL cholesterol (95% CI 1.7-3.6).

CONCLUSIONS: Our study has shown high prevalence of traditional risk factors and silent myocardial ischemia in type 2 diabetic patients, with the importance of SPECT imaging in selected diabetes type 2 patients. The study highlights the importance of screening for carotid atherosclerosis, which may be useful to identify diabetic patients at higher risk for coronary artery disease..

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PMID: 28198536 [Indexed for MEDLINE]

Ann Endocrinol (Paris). 2017 Feb;78(1):14-19.

Usefulness of a systematic screening of carotid atherosclerosis in asymptomatic people with type 2 diabetes for cardiovascular risk reclassification.

Helfre M, Grange C, Riche B, Maucort-Boulch D, Thivolet C, Vouillarmet J.

AIMS: Routine screening of carotid atherosclerosis lesions is frequently suggested for people with type 2 diabetes, the presence of a carotid lesion being associated with a significant increase risk for vascular events. However, the impact of this strategy on medical management is not validated. We herein question the usefulness of such screening.

METHODS: We assessed the prevalence and severity of carotid lesions in 337 consecutive people with type 2 diabetes without known cardiovascular disease who underwent a systematic carotid duplex ultrasonography. We analyzed whether the results of duplex ultrasonography allowed reclassification of cardiovascular risk level relative to the most recent international recommendations on diabetes and modified therapy.

RESULTS: We found that 35.9% of people had no atherosclerotic lesion. Prevalence of carotid stenosis<20%, between 20 and 50% and ≥50% were 32.9%, 28.4% and 2.7% respectively. Regarding the use of statins and LDL-C target, the result of carotid duplex ultrasonography allowed to reclassify respectively 11.8% to 55.2% of the cohort in a higher cardiovascular risk level. For the indication of antiplatelet agent, reclassification in a higher risk level concerned 6.8% of the patients. No subject had an indication of carotid revascularization.

CONCLUSIONS: Carotid atherosclerosis is frequent in asymptomatic people with type 2 diabetes in primary cardiovascular prevention. Screening for carotid atherosclerosis by duplex ultrasonography seems useful to redefine the level of cardiovascular risk.

DOI: 10.1016/j.ando.2016.12.001
PMID: 28185650 [Indexed for MEDLINE]

BMC Neurol. 2017 Feb 6; 17(1):24.

Randomized controlled trial of a coordinated care intervention to improve risk factor control after stroke or transient ischemic attack in the safety net: Secondary stroke prevention by Uniting Community and hronic care model teams Early to End Disparities (SUCCEED).

Towfighi A, Cheng EM, Ayala-Rivera M, McCreath H, Sanossian N, Dutta T, Mehta B, Bryg R, Rao N, Song S, Razmara A, Ramirez M, Sivers-Teixeira T, Tran J, Mojarro-Huang E, Montoya A, Corrales M, Martinez B, Willis P, Macias M, Ibrahim N, Wu S, Wacksman J, Haber H, Richards A, Barry F, Hill V, Mittman B, Cunningham W, Liu H, Ganz DA, Factor D, Vickrey BG.

BACKGROUND: Recurrent strokes are preventable through awareness and control of risk factors such as hypertension, and through lifestyle changes such as healthier diets, greater physical activity, and smoking cessation. However, vascular risk factor control is frequently poor among stroke survivors, particularly among socio-economically disadvantaged blacks, Latinos and other people of color. The Chronic Care Model (CCM) is an effective framework for multi-component interventions aimed at improving care processes and outcomes for individuals with chronic disease. In addition, community health workers (CHWs) have played an integral role in reducing health disparities; however, their effectiveness in reducing vascular risk among stroke survivors remains unknown. Our objectives are to develop, test, and assess the economic value of a CCM-based intervention using an Advanced Practice Clinician (APC)-CHW team to improve risk factor control after stroke in an under-resourced, racially/ethnically diverse population.

METHODS/DESIGN: In this single-blind randomized controlled trial, 516 adults (≥40 years) with an ischemic stroke, transient ischemic attack or intracerebral hemorrhage within the prior 90 days are being enrolled at five sites within the Los Angeles County safety-net setting and randomized 1:1 to intervention vs usual care. Participants are excluded if they do not speak English, Spanish, Cantonese, Mandarin, or Korean or if they are unable to consent. The intervention includes a minimum of three clinic visits in the healthcare setting, three home visits, and Chronic Disease Self-Management Program group workshops in community venues. The primary outcome is blood pressure (BP) control (systolic BP <130 mmHg) at 1 year. Secondary outcomes include: (1) mean change in systolic BP; (2) control of other vascular risk factors including lipids and hemoglobin A1c, (3) inflammation (C reactive protein [CRP]), (4) medication adherence, (5) lifestyle factors (smoking, diet, and physical activity), (6) estimated relative reduction in risk for recurrent stroke or myocardial infarction (MI), and (7) cost-effectiveness of the intervention versus usual care.

DISCUSSION: If this multi-component interdisciplinary intervention is shown to be effective in improving risk factor control after stroke, it may serve as a model that can be used internationally to reduce race/ethnic and socioeconomic disparities in stroke in resource-constrained settings.
TRIAL REGISTRATION: ClinicalTrials.gov Identifier NCT01763203 .

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PMCID: PMC5294765
PMID: 28166784 [Indexed for MEDLINE]

Medicine (Baltimore). 2017 Feb;96(5):e5868.

A lower baseline glomerular filtration rate predicts high mortality and newly cerebrovascular accidents in acute ischemic stroke patients.

Dong K, Huang X, Zhang Q, Yu Z, Ding J, Song H.

Chronic kidney disease (CKD) is gradually recognized as an independent risk factor for cardiovascular and cardio-/cerebrovascular disease. This study aimed to examine the association of the estimated glomerular filtration rate (eGFR) and clinical outcomes at 3 months after the onset of ischemic stroke in a hospitalized Chinese population. Totally, 972 patients with acute ischemic stroke were enrolled into this study. Modified of Diet in Renal Disease (MDRD) equations were used to calculate eGFR and define CKD. The site and degree of the stenosis were examined. Patients were followed-up for 3 months. Endpoint events included all-cause death and newly ischemic events. The multivariate logistic model was used to determine the association between renal dysfunction and patients' outcomes.Of all patients, 130 patients (13.4%) had reduced eGFR (<60 mL/min/1.73 m), and 556 patients had a normal eGFR (≥90 mL/min/1.73 m). A total of 694 patients suffered from cerebral artery stenosis, in which 293 patients only had intracranial artery stenosis (ICAS), 110 only with extracranial carotid atherosclerotic stenosis (ECAS), and 301 with both ICAS and ECAS. The patients with eGFR <60 mL/min/1.73m had a higher proportion of death and newly ischemic events compared with those with a relatively normal eGFR. Multivariate analysis revealed that a baseline eGFR <60 mL/min/1.73 m increased the risk of mortality by 3.089-fold and newly ischemic events by 4.067-fold. In further analysis, a reduced eGFR was associated with increased rates of mortality and newly events both in ICAS patients and ECAS patients. However, only an increased risk of newly events was found as the degree of renal function deteriorated in ICAS patients (odds ratio = 8.169, 95% confidence interval = 2.445-14.127).A low baseline eGFR predicted a high mortality and newly ischemic events at 3 months in ischemic stroke patients. A low baseline eGFR was also a strong independent predictor for newly ischemic events in ICAS patients.

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PMCID: PMC5293425
PMID: 28151862 [Indexed for MEDLINE]

Medicine (Baltimore). 2017 Jan;96(4):e5999.

Prevalence and risk factors for atherosclerotic carotid stenosis and plaque: A population-based screening study.

Woo SY, Joh JH, Han SA, Park HC.

Atherosclerotic carotid stenosis (ACS) is a major cause of ischemic stroke. Screening for asymptomatic ACS is important to identify the patients who require longitudinal surveillance, medication, or endovascular surgery. The aim of this study was to assess the prevalence and risk factors for ACS and carotid plaque (CP) in Korea using a population-based screening study. We recruited participants during visits to several community welfare centers in Korea. The baseline characteristics of the study population were collected. All patients underwent duplex ultrasonography to examine their bilateral carotid arteries. ACS was defined as the presence of plaque with ≥50% vessel diameter reduction and peak systolic velocity (PSV) ≥125 cm/s or PSV ratio ≥2.0. CP was defined as the presence of plaque with <50% vessel diameter reduction. The Mann-Whitney test, χ test, Fisher exact test, and logistic regression were used in the statistical analysis. A total of 3030 participants were enrolled in this study (male 43.7% and female 56.3%). The prevalence of ACS and CP was 1.1% and 5.7%, respectively. Significant risk factors for CP included age ≥80 years (odds ratio [OR], 8.11; 95% confidence interval [CI], 3.45-18.93), male sex (OR, 2.16; 95% CI, 1.29-3.61), hypertension (OR, 1.72; 95% CI, 1.21-2.45), and hyperlipidemia (OR, 1.84; 95% CI, 1.30-2.62). The presence of ACS was significantly associated with age (OR, 1.07; 95% CI, 1.03-1.12), hypertension (OR, 3.16; 95% CI, 1.34-7.46), and being an ex-smoker (OR, 6.81; 95% CI, 1.66-27.93) or current smoker (OR, 6.97; 95% CI, 1.78-27.31) after adjusting for confounding factors. This population-based screening study revealed that ACS was uncommon and had a prevalence of 1.1% in the study population. Age, hypertension, and smoking were risk factors for ACS. Further investigations into the prevalence and risk factors of ACS are required, as are studies on the cost-effectiveness of a national screening program.

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PMCID: PMC5287981
PMID: 28121957 [Indexed for MEDLINE]

Diabetes Res Clin Pract. 2017 Feb;124:93-101.

Sleep duration and smoking are associated with coronary heart disease among US adults with type 2 diabetes: Gender differences.

Li L, Gong S, Xu C, Zhou JY, Wang KS.

AIMS: The associations of moderate alcohol consumption, sleep duration, and tobacco smoking with coronary heart disease (CHD) among patients with type 2 diabetes mellitus (T2D) are not clearly clarified. The aims of the study were to evaluate the associations of lifestyle factors, hypertension, obesity, depression and sleep duration with CHD development among patients with T2D, and particularly, to examine the gender differences in risk factors for CHD.

METHODS: A total of 2335 T2D adults were selected from the 2012 National Health Interview Survey. Weighted univariate and multiple logistic regression analyses were used to estimate the odds ratios with 95% confidence intervals.

RESULTS: The CHD prevalence among patients with T2D was 14.2% (18.1% and 10.4% for males and females, respectively), which increased with age (10.3% and 19.6% for age groups 18-64 and 65+, respectively). After adjusting for other factors, weighted logistic regression analyses showed that CHD among patients with T2D was significantly associated with being male, older age, past smoking, long sleep duration, hypertension, and high cholesterol level. Furthermore, the significant association of older age, past smoking, hypertension and high cholesterol level were observed particularly in males, while the association of long sleep duration with CHD was only observed in females. Hypertension was associated with CHD for both genders.

CONCLUSIONS: Gender, age, past smoking, long sleep duration, hypertension and high cholesterol level were significantly associated with CHD among T2D patients; however, such associations differed by gender. Such gender disparities should be considered in the prevention and treatment of T2D.

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PMID: 28119195 [Indexed for MEDLINE]

Clin Obes. 2017 Apr;7(2):77-85.

Association between obesity and heart failure symptoms in male and female patients.

Heo S, Moser DK, Pressler SJ, Dunbar SB, Lee KS, Kim J, Lennie TA.

In patients with heart failure (HF), higher body mass index (BMI) has been associated with lower rates of hospitalization and mortality (obesity paradox). Symptoms are antecedents of hospitalizations, but little is known about the relationship between BMI and symptoms and gender differences.

To examine the association of BMI with symptoms in male and female patients with HF, controlling for covariates (sample characteristics, depressive symptoms and sodium intake). In this cross-sectional correlational study, patients (N = 247) provided data on BMI, symptoms and covariates. BMI was categorized into four groups: normal/underweight (<25 kg/m(2)), overweight (25-29.9 kg/m(2)), obese I (30-34.9 kg/m(2)) and obese II/III (≥35 kg/m(2)). General linear regression was used to analyse the data.

The Obese II/III group had more severe HF symptoms than other groups only in male patients. In male patients, older age, Caucasian race, more comorbidities and more severe depressive symptoms were also associated with more severe symptoms. In female patients, more severe depressive symptoms, more comorbidities and higher sodium intake were associated with more severe symptoms. The obesity paradox does not fully extend to symptoms, and gender has a role in the relationship between obesity and symptoms.

DOI: 10.1111/cob.12179
PMID: 28117927 [Indexed for MEDLINE]

Arch Iran Med. 2017 Jan;20(1):55-59.

Causal Effects of Intensive Lifestyle and Metformin Interventions on Cardiovascular Disease Risk Factors in Pre-Diabetic People: An Application of G-Estimation.

Salimi Y, Fotouhi A, Mohammad K, Mansournia N, Mansournia MA.

BACKGROUND: In the presence of non-adherence, intention-to-treat analysis preserves randomization, but does not lead to a valid comparison of outcome between the assigned groups. Using a reanalysis of Diabetes Prevention Program, this study aimed to estimate the causal effect of treatment with intensive lifestyle intervention or metformin vs. placebo on blood pressure and lipid profile using G-estimation after accounting for non-adherence.

METHODS: The Diabetes Prevention Program randomized 3,052 pre-diabetic individuals to metformin (N = 1015), placebo (N = 1014), or an intensive lifestyle intervention (N = 1023). G-estimation was used to estimate the causal effect of intensive lifestyle intervention or metformin vs. placebo on blood pressure and lipid profile in 2,973 patients who had adherence data. For comparison, we also performed the standard intention-to-treat analysis.

RESULTS: The G-estimation results showed that intensive lifestyle substantially improves systolic and diastolic blood pressure and lipid profile. The G-estimates of the effects of metformin vs. placebo as well as intensive lifestyle intervention vs. metformin on blood pressure and lipid profile were also stronger than the intention-to-treat effect estimates.

CONCLUSION: G-estimation suggests that intensive lifestyle modification improves known risk factors for cardiovascular disease, including systolic blood pressure, diastolic blood pressure, triglyceride, and HDL levels more than what standard ITT analysis suggests. Adherence to the assigned treatment should be measured in all randomized trials, and G-estimation should be the standard analysis of randomized trials with substantial non-adherence.

DOI: 0172001/AIM.0012
PMID: 28112533 [Indexed for MEDLINE]

Blood Press. 2017 Jun;26(3):166-173.

Hypertension is associated with increased mortality in patients with ischaemic heart disease after revascularization with percutaneous coronary intervention – a report from SCAAR.

Saluveer O, Redfors B, Angerås O, Dworeck C, Haraldsson I, Ljungman C, Petursson P, Odenstedt J, Ioanes D, Lundgren P, Völz S, Råmunddal T, Andersson B, Omerovic E, Bergh N.

BACKGROUND: The prognostic role of hypertension on long-term survival after percutaneous coronary intervention (PCI) is limited and inconsistent. We hypothesize that hypertension increases long-term mortality after PCI.

METHODS: We analyzed data from SCAAR (Swedish Coronary Angiography and Angioplasty Registry) for all consecutive patients admitted coronary care units in Sweden between January 1995 and May 2013 and who underwent PCI due to ST-elevation myocardial infarction (STEMI), non-ST-elevation myocardial infarction (NSTEMI)/unstable angina (UA) or stable angina pectoris. We used Cox proportional-hazards regression for statistical modelling on complete-case data as well as on imputed data sets. We used interaction test to evaluate possible effect-modulation of hypertension on risk estimates in several pre-specified subgroups: age categories, gender, diabetes, smoking and indication for PCI (STEMI, NSTEMI/UA and stable angina).

RESULTS: During the study period, 175,892 consecutive patients underwent coronary angiography due to STEMI, NSTEMI/UA or stable angina. 78,100 (44%) of these had hypertension. Median follow-up was 5.5 years. After adjustment for differences in patient's characteristics, hypertension was associated with increased risk for mortality (HR 1.12, 95% CI 1.09-1.15, $p < .001$). In subgroup analysis, risk was highest in patients less than 65 years, in smokers and in patients with STEMI. The risk was lowest in patients with stable angina ($p < .001$ for interaction test).

CONCLUSION: Hypertension is associated with higher mortality in patients with STEMI, NSTEMI/UA or stable angina who are treated with PCI.

DOI: 10.1080/08037051.2016.1270162
PMID: 28092977 [Indexed for MEDLINE]

Circ J. 2017 Jan 25; 81(2):185-194.

Prognostic Impact of Atrial Fibrillation and New Risk Score of Its Onset in Patients at High Risk of Heart Failure - A Report From the CHART-2 Study.

Yamauchi T, Sakata Y, Miura M, Onose T, Tsuji K, Abe R, Oikawa T, Kasahara S, Sato M, Nochioka K, Shiroto T, Takahashi J, Miyata S, Shimokawa H; CHART-2 Investigators.

BACKGROUND: The prognostic impact of atrial fibrillation (AF) among patients at high risk for heart failure (HF) remains unclear. In addition, there is no risk estimation model for AF development in these patients.

Methods and Results: The present study included 5,382 consecutive patients at high risk of HF enrolled in the CHART-2 Study (n=10,219). At enrollment, 1,217 (22.6%) had AF, and were characterized, as compared with non-AF patients, by higher age, lower estimated glomerular filtration rate, higher B-type natriuretic peptide (BNP) level and lower left ventricular ejection fraction. A total of 116 non-AF patients (2.8%) newly developed AF (new AF) during the median 3.1-year follow-up. AF at enrollment was associated with worse prognosis for both all-cause death and HF hospitalization (adjusted hazard ratio (aHR) 1.31, P=0.027 and aHR 1.74, P=0.001, for all-cause death and HF hospitalization, respectively) and new AF was associated with HF hospitalization (aHR 4.54, P<0.001). We developed a risk score with higher age, smoking, pulse pressure, lower eGFR, higher BNP, aortic valvular regurgitation, LV hypertrophy, and left atrial and ventricular dilatation on echocardiography, which effectively stratified the risk of AF development with excellent accuracy (AUC 0.76).

CONCLUSIONS: These results indicated that AF is associated with worse prognosis in patients at high risk of HF, and our new risk score may be useful to identify patients at high risk for AF onset.

DOI: 10.1253/circj.CJ-16-0759
PMID: 28090009 [Indexed for MEDLINE]

Cardiol Young. 2017 Jan;27(S1):S94-S100.

Morbidities in the ultra-athlete and marathoner.

Cunningham TC, Maghrabi K, Sanatani S.

The cardiovascular benefits of habitual exercise are well documented. In the current era, more of the population is exceeding the recommendations for physical activity as the popularity of endurance events increases. Recent data have proposed a U-shaped relationship between exercise intensity and cardiovascular outcomes. Regular participation in endurance activities has been shown to result in structural and functional changes in the heart. This re-modelling may be the substrate for cardiac dysfunction or arrhythmias. The risk of sudden cardiac death may also be elevated; however, in most cases of sudden cardiac death, the cause can be linked to an underlying cardiac pathology where exercise acted as the trigger for a lethal arrhythmia. This article serves to review whether excessive exercise may result in harm in some athletes.

DOI: 10.1017/S1047951116002304
PMID: 28084966 [Indexed for MEDLINE]

Clin Chim Acta. 2017 Mar;466:54-60.

Associations of the fatty liver and hepatic steatosis indices with risk of cardiovascular disease: Interrelationship with age.

Kunutsor SK, Bakker SJ, Blokzijl H, Dullaart RP.

BACKGROUND: The fatty liver index (FLI) and the hepatic steatosis index (HSI), are biomarker-based algorithms developed as proxies for non-alcoholic fatty liver disease (NAFLD). We assessed associations of FLI and HSI with cardiovascular disease (CVD) risk.

MATERIALS AND METHODS: The FLI and HSI were estimated at baseline in the PREVEND cohort involving 6340 participants aged 28-75years without pre-existing CVD.

RESULTS: During a median follow-up of 10.5years, 631 CVD events occurred. In age-and sex-adjusted analysis, the hazard ratio (HR) (95% CI) for CVD comparing FLI≥60 versus FLI<30 was 1.53 (1.25-1.88); which was attenuated to 0.89 (0.70-1.13) on adjustment for conventional cardiovascular risk factors. The association remained absent after additional adjustment for potential confounders 0.85 (0.65-1.11). Comparing HSI>36 versus HSI<30, the corresponding adjusted HRs were 1.29 (1.02-1.65), 0.84 (0.65-1.09) and 0.79 (0.55-1.13) respectively. Subgroup analyses suggested a positive association in younger participants (<50years) for FLI and inverse associations in older participants (≥50years) for both indices (P for interaction for all=0.001).

CONCLUSION: Current data suggest age interactions in the association of NAFLD (as assessed by FLI or HSI) with CVD risk in a general Caucasian population.

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PMID: 28082024 [Indexed for MEDLINE]

Medicine (Baltimore). 2017 Jan;96(2):e5874.

Waist-to-height ratio is the best anthropometric predictor of hypertension: A population-based study with women from a state of northeast of Brazil.

Caminha TC, Ferreira HS, Costa NS, Nakano RP, Carvalho RE, Xavier AF Jr, Assunção ML.

The WHO recommends the use of some anthropometric parameters as a screening resource for individuals under cardiometabolic risk. However, in the validation of these indicators, Brazilian women were not included. These women have different anthropometric profile compared to women who integrated the samples of the validation studies. We aimed to verify the accuracy of anthropometric Indicators as a resource for the screening of women with hypertension. A cross-sectional study, with a probability sample of 3143 women (20-49 years) from the state of Alagoas (northeast of Brazil), was carried out. Hypertension was identified by systolic blood pressure (SBP) ≥140 mm Hg and/or diastolic BP ≥90 mm Hg and/or regular use of antihypertensive drugs. The anthropometric indicators analyzed were BMI, waist circumference, waist-to-hip ratio, waist-to-height ratio (WHtR), body fat percentage, and conicity index. The accuracy definition of the indicators and the identification of best cut-off points were carried out on the basis of ROC curve analysis and Youden index, respectively. The prevalence of hypertension was 21.8%. All indicators used in hypertension identification had area under the ROC curve (AUC) >0.5. The WHtR with cut-off point of 0.54 was the best performance indicator (AUC = 0.72; P < 0.05; sensitivity = 67%, specificity = 66%). The WHtR with cut-off point of 0.54 has constituted the most accurate indicator in the screening of women with hypertension.

In the absence of specific studies and considering the largest ethnic proximity and environmental/epidemiological similarity, the findings now obtained can be extended to women of other Brazilian states, especially those in the Northeastern region.

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Metabolic syndrome, hypertension, and nervous system injury: Epidemiological correlates.

Ricci G, Pirillo I, Tomassoni D, Sirignano A, Grappasonni I.

Metabolic syndrome (MetS) is a common and complex disorder combining hypertension, obesity, dyslipidemia, and insulin resistance. MetS represents a risk factor for changes in cognitive functions in older age, and several studies have suggested that MetS may be linked to dementia. This article reviews the main evidences about the relationship between MetS and neurodegenerative disease.
Starting from an epidemiological point of view, the article analyzes medico-social aspects related to MetS, considering the reduction of work capacity and the condition of disability that it involves. Some authors affirm that on the basis of current Italian legislation, it is possible to consider the syndrome as a disability. This is because all the diseases that make up MetS are high-risk clinical pathological conditions. For these reasons, a joint action is required to contain the incidence of MetS, the high social costs, and the loss of productivity related to the syndrome. In conclusion, healthcare initiatives could be adopted in order to increase the understanding of the pathogenic contributions of each element on MetS and how they can be modified. These actions will be useful to reduce healthcare costs and can lead to more effective prevention of metabolic disease, thus promoting good health.

ABBREVIATIONS: MetS: Metabolic syndrome; WHO: World Health Organization; CVD: cerebrovascular diseases; AD: Alzheimer's Disease; VaD: Vascular Dementia; IDF: International Diabetes Federation; T2DM: type 2 diabetes mellitus; CAD: coronary artery disease; MCI: mild cognitive impairment; NCDs: Non Communicable Diseases; BMI: Body Mass Index; ICIDH: International classification of impairments, disabilities and handicaps.

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Int J Artif Organs. 2017 Jan 13;39(11):563-569.

Sleep quality and risk factors of atherosclerosis in predialysis chronic kidney disease.

Guney I, Akgul YS, Gencer V, Aydemir H, Aslan U, Ecirli S.

INTRODUCTION: Chronic kidney disease (CKD) patients have more frequent sleep disorders and cardiovascular disease than normals. Since arterial stiffness as a risk factor of atherosclerosis can be evaluated with pulse wave velocity (PWV), we aimed to investigate the prevalance of sleep quality (SQ) and the relationship between SQ and risk factors of atherosclerosis and whether there is a relationship between SQ and PWV (the indicator of arterial stiffness) in predialysis CKD patients.

METHODS: This cross-sectional study was carried out in CKD patients followed at the Nephrology Department in Konya, Turkey, between November 2014 and March 2015. A total of 484 CKD patients were screened. Of the 484 patients, 285 patients were excluded. The remaining 199 CKD patients without cardiovascular disease at stage 3, 4, and 5 (predialysis) were included in the final study. The SQ of the patients was evaluated by the Pittsburgh Sleep Quality Index (PSQI). PWV was measured by using a single-cuff arteriography device (Mobil-O-Graph PWA, a model pulse wave analysis device; IEM).

RESULTS: A total of 199 predialysis CKD patients were included in the study, 73 of whom (36.7 %) were 'poor sleepers' (global PSQI >5). Patients with poor SQ were older than those with good SQ (p = 0.077). SQ was worse in female patients compered to male patients (p = 0.001). SQ was worse in obese patients. As laboratory parameters, serum phosphorus, LDL cholesterol, and triglycerides levels correlated positively with SQ (respectively; r = 0.245, p& 0.001; r = 0.142, p = 0.049; r = 0.142, p = 0.048). The indicator of arterial stiffness, PWV, was higher in patients with poor SQ (p = 0.033). Hyperphosphatemia and female gender are determined as risk factors for poor SQ in multivariate analysis (p = 0.049, ExpB = 1.477; p = 0.009, ExpB = 0,429, respectively).

CONCLUSIONS: Our study showed for the first time that there is a relationship between SQ and risk factors of atherosclerosis in predialysis CKD patients.

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PMID: 28009416 [Indexed for MEDLINE]

Appl Physiol Nutr Metab. 2017 Jan;42(1):39-45.

Dietary intake and prospective changes in cardiometabolic risk factors in children and youth.

Setayeshgar S, Ekwaru JP, Maximova K, Majumdar SR, Storey KE, McGavock J, Veugelers PJ.

Only few studies examined the effect of diet on prospective changes in cardiometabolic (CM) risk factors in children and youth despite its importance for understanding the role of diet early in life for cardiovascular disease in adulthood. To test the hypothesis that dietary intake is associated with prospective changes in CM risk factors, we analyzed longitudinal observations made over a period of 2 years among 448 students (aged 10-17 years) from 14 schools in Canada. We applied mixed effect regression to examine the associations of dietary intake at baseline with changes in body mass index, waist circumference (WC), systolic and diastolic blood pressure (SBP and DBP), and insulin sensitivity score between baseline and follow-up while adjusting for age, sex, and physical activity. Dietary fat at baseline was associated with increases in SBP and DBP z scores (per 10 g increase in dietary fat per day: $\beta = 0.03$; $p < 0.05$) and WC ($\beta = 0.31$ cm; $p < 0.05$) between baseline and follow-up. Every additional gram of sodium intake at baseline was associated with an increase in DBP z score of 0.04 ($p < 0.05$) between baseline and follow-up. Intake of sugar, vegetables and fruit, and fibre were not associated with changes in CM risk factors in a statistically significant manner.

Our findings suggest that a reduction in the consumption of total dietary fat and sodium may contribute to the prevention of excess body weight and hypertension in children and youth, and their cardiometabolic sequelae later in life.

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PMID: 27959641 [Indexed for MEDLINE]

Acta Obstet Gynecol Scand. 2017 Feb;96(2):243-250.

Risk factors for recurrence of hypertensive disorders of pregnancy, a population-based cohort study.

Ebbing C, Rasmussen S, Skjaerven R, Irgens LM.

INTRODUCTION: Hypertensive disorders of pregnancy (HDP) tend to recur from one pregnancy to the next. The aims of the study were to assess the recurrence risk according to type of HDP defined by gestational age at birth and to examine whether recurrence is associated with the following additional risk factors for HDP: maternal age, smoking, inter-delivery interval, diabetes, body mass index, and fetal growth restriction, and to assess temporal trends in these associations.

MATERIAL AND METHODS: All women with two singleton births in the Medical Birth Registry of Norway 1967-2012 (n = 742 980) were included in this population-based cohort study. Logistic regression was used to calculate odds ratios for the risk of recurrent HDP according to type of HDP.
RESULTS: The highest odds ratio of recurrence was observed for the same type of HDP based on gestational age at delivery. After gestational hypertension and term preeclampsia, the risk for the same type to recur increased 10-fold, whereas after late and early preterm preeclampsia, the risk increased 27- and 97-fold, respectively. The recurrence of early preterm preeclampsia was less influenced by additional risk factors compared with term HDP. Recurrence of early preterm HDP was significantly lower from 1993 onwards.

CONCLUSIONS: Recurrent HDP tended to be of the same type as the previous HDP. Risk of recurrence associated with additional risk factors was observed particularly after term. The odds ratio of recurrence of early preterm HDP was significantly lower from 1993 onwards.

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PMID: 27874979 [Indexed for MEDLINE]

Yonsei Med J. 2017 Jan;58(1):114-122.

Increased Risk of Cardiovascular Events in Stroke Patients Who had Not Undergone Evaluation for Coronary Artery Disease.

Kim YD, Song D, Nam HS, Choi D, Kim JS, Kim BK, Chang HJ, Choi HY, Lee K, Yoo J, Lee HS, Nam CM, Heo JH.

PURPOSE: Although asymptomatic coronary artery occlusive disease is common in stroke patients, the long-term advantages of undergoing evaluation for coronary arterial disease using multi-detector coronary computed tomography (MDCT) have not been well established in stroke patients. We compared long-term cardio-cerebrovascular outcomes between patients who underwent MDCT and those who did not.

MATERIALS AND METHODS: This was a retrospective study in a prospective cohort of consecutive ischemic stroke patients. Of the 3117 patients who were registered between July 2006 and December 2012, MDCT was performed in 1842 patients [MDCT (+) group] and not in 1275 patients [MDCT (-) group]. Occurrences of death, cardiovascular events, and recurrent stroke were compared between the groups using Cox proportional hazards models and propensity score analyses.

RESULTS: During the mean follow-up of 38.0±24.8 months, 486 (15.6%) patients died, recurrent stroke occurred in 297 (9.5%), and cardiovascular events occurred in 60 patients (1.9%). Mean annual risks of death (9.34% vs. 2.47%), cardiovascular events (1.2% vs. 0.29%), and recurrent stroke (4.7% vs. 2.56%) were higher in the MDCT (-) group than in the MDCT (+) group. The Cox proportional hazards model and the five propensity score-adjusted models consistently demonstrated that the MDCT (-) group was at a high risk of cardiovascular events (hazard ratios 3.200, 95% confidence interval 1.172-8.735 in 1:1 propensity matching analysis) as well as death. The MDCT (-) group seemed to also have a higher risk of recurrent stroke.

CONCLUSION: Acute stroke patients who underwent MDCT experienced fewer deaths, cardiovascular events, and recurrent strokes during follow-up.

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PMCID: PMC5122626
PMID: 27873503 [Indexed for MEDLINE]

Yonsei Med J. 2017 Jan;58(1):75-81.

The Impact of Diabetes Mellitus on Vascular Biomarkers in Patients with End-Stage Renal Disease.

Moon J, Lee CJ, Lee SH, Kang SM, Choi D, Yoo TH, Park S.

PURPOSE: Diabetes mellitus (DM) is the most common cause of end-stage renal disease (ESRD) and an important risk factor for cardiovascular (CV) disease. We investigated the impact of DM on subclinical CV damage by comprehensive screening protocol in ESRD patients.

MATERIALS AND METHODS: Echocardiography, coronary computed tomography angiogram, 24-h ambulatory blood pressure monitoring, and central blood pressure with pulse wave velocity (PWV) were performed in 91 ESRD patients from the Cardiovascular and Metabolic disease Etiology Research Center-HIgh risk cohort.

RESULTS: The DM group (n=38) had higher systolic blood pressure than the non-DM group (n=53), however, other clinical CV risk factors were not different between two groups. Central aortic systolic pressure (148.7±29.8 mm Hg vs. 133.7±27.0 mm Hg, p= 0.014), PWV (12.1±2.7 m/s vs. 9.4±2.1 m/s, p<0.001), and early mitral inflow to early mitral annulus velocity (16.7±6.4 vs. 13.7±5.9, p=0.026) were higher in the DM group. Although the prevalence of coronary artery disease (CAD) was not different between the DM and the non-DM group (95% vs. 84.4%, p=0.471), the severity of CAD was higher in the DM group (p=0.01). In multivariate regression analysis, DM was an independent determinant for central systolic pressure (p=0.011), PWV (p<0.001) and the prevalence of CAD (p=0.046).

CONCLUSION: Diabetic ESRD patients have higher central systolic pressure and more advanced arteriosclerosis than the non-DM control group. These findings suggest that screening for subclinical CV damage may be helpful for diabetic ESRD patients.

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Why would serum phosphorus correlate with cardiovascular risk, and how is the clinician supposed to use this information?

Lederer E.

Numerous recent studies have demonstrated an association between serum phosphorus and cardiovascular risk, even in individuals with normal kidney function and with serum phosphorus levels considered within the acceptable range. Whether serum phosphorus serves as a biomarker, as a causative agent, or both remains unclear. Additionally, the impact of other important considerations, such as the time of day when the phosphorus is measured, the diet of the individual, and the age of the individual, on interpretation of this association has not been determined. Currently, serum phosphorus cannot be used systematically as an independent cardiovascular risk factor but may be an important adjunctive factor in analyzing cardiovascular risk. More importantly, understanding the basis for the association between serum phosphorus and cardiovascular risk will likely yield new insights into fundamental mechanisms of cardiovascular disease.

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PMID: 27841147 [Indexed for MEDLINE]

Scand J Public Health. 2017 Feb;45(1):50-56.

Ideal cardiovascular health and psychosocial risk factors among Finnish female municipal workers.

Veromaa V, Kautiainen H, Saxen U, Malmberg-Ceder K, Bergman E, Korhonen PE.

AIMS: Ideal cardiovascular health has been defined by the American Heart Association as the absence of disease and the presence of seven key health factors and behaviours. However, little is known about the mental aspects associated with ideal cardiovascular health metrics. The objective of this study was to assess the relationships between psychosocial risk factors and ideal cardiovascular health metrics among Finnish women at municipal work units.

METHOD: A cross-sectional study was conducted in Finland among 732 female employees (mean ±SD age 48±10 years) from ten work units in 2014. Ideal cardiovascular health metrics were evaluated with a physical examination, laboratory tests, medical history and self-administrated questionnaires. Psychosocial risk factors (social isolation, stress, depressive symptoms, anxiety, hostility and type D personality) were assessed with core questions as suggested by the European Society of Cardiology.

RESULTS: The prevalence of having 5-7 ideal cardiovascular health metrics was 183 (25.0%), of whom 54.1% had at least one psychosocial risk factor. Anxiety (31.3%), work stress (30.7%) and type D personality (26.1%) were the most prevalent of the psychosocial risk factors. The prevalence of depressive symptoms ($p<0.001$) and type D personality ($p=0.049$) decreased linearly according to the sum of ideal cardiovascular health metrics after adjustment for age and years of education.

CONCLUSIONS: Even women with good cardiovascular health are affected by psychosocial risk factors at municipal work units. Although the association is possibly bidirectional, screening and treating depression and dealing with type D personality might be crucial in improving cardiovascular health among women.

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PMID: 27821483 [Indexed for MEDLINE]

Ann Vasc Surg. 2017 Feb;39:301-311

Management of Modifiable Vascular Risk Factors Improves Late Survival following Abdominal Aortic Aneurysm Repair: A Systematic Review and Meta-Analysis.

Khashram M, Williman JA, Hider PN, Jones GT, Roake JA.

BACKGROUND: The main determinants of survival following abdominal aortic aneurysm (AAA) repair are preexisting risk factors rather than the method of repair chosen. The main aim of this meta-analysis was to assess the effect of modifiable risk factors on late survival following AAA repair.

METHODS: Electronic databases were searched to identify all relevant articles reporting the influence of modifiable risk factors on long-term survival (≥1 year) following elective open aneurysm repair and endovascular aneurysm repair.

RESULTS: Twenty-four studies which comprised 53,118 patients, published between 1989 and 2015, were included in the analysis. The use of statin, aspirin, beta-blockers, and a higher hemoglobin level was all significant predictors of improved survival following repair with a hazard ratio (HR) and 95% confidence interval (CI) of 0.75 (0.70-0.80), 0.81 (0.73-0.89), 0.75 (0.61-0.93), and 0.84 (0.74-0.96), respectively. Smoking history and uncorrected coronary disease were associated with a worse long-term survival of HR 1.27 (95% CI 1.07-1.51) and HR 2.59 (95% CI 1.14-5.88), respectively.

CONCLUSIONS: Addressing cardiovascular risk factors in patients preoperatively improves long-term survival following AAA repair. Global strategies to improve risk factor modifications in these patients are warranted to optimize long-term outcomes.

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PMID: 27666804 [Indexed for MEDLINE]

Diabetes Metab Syndr. 2017 Jan - Mar;11(1):43-46.

Metabolic syndrome and its components in postmenopausal women living in southern Italy, Apulia region.

Maiello M, Zito A, Ciccone MM, Palmiero P.

OBJECTIVES: The goal of our study was to determine the prevalence of metabolic syndrome (MetS) and all its components, in a population of postmenopausal women aged over 45 years, consecutively accessed to our Heart Station, during 2014, for their first cardiac examination, furthermore to estimate their cardiovascular risk and the achievement of target blood values of main risk factors, according to current Guidelines.

METHODS: We screened 1257 postmenopausal women. MetS was assessed according to the National-Cholesterol-Education-Program-Adult-Treatment-Panel III definition. Cardiovascular risk was calculated by the Systematic Coronary Risk Evaluation (<65 years).

RESULTS: MetS was assessed on 834 women (66.4%). Prevalence of each component was: hypertension on 767 women (91.9%), central obesity 758 women (90.9%), low high-density lipoproteins cholesterol (HDLc) increased levels 612 women (73.3%), high triglyceride levels 428 women (51.3%), glucose levels higher than 110mg/dl or diabetes 404 women (48.5%). Cardiovascular risk was moderate until 65 years, but it increases after. Metabolic control in postmenopausal women was poor for glucose, only 82 women (9.8%) presented glucose levels lower than 110mg/dl, it was better for systolic blood pressure, that was normal in 564 women (67.6%) and worse for lipid levels.

CONCLUSION: The prevalence of metabolic syndrome in our population of postmenopausal women is high. Hypertension and central obesity are the more common components. The cardiovascular risk is moderate-high, the achievement of target values for glycemic and lipid levels is unsatisfactory, while systolic blood pressure is enough well controlled but however it is mandatory to improve this goal. An early MetS diagnosis and an early educational intervention are useful to decrease cardiovascular risk of postmenopausal women affected by metabolic syndrome.

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PMID: 27596043 [Indexed for MEDLINE]

Clin Res Cardiol. 2017 Feb;106(2):96-104.

Factors independently associated with cardiac troponin I levels in young and healthy adults from the general population.

Bossard M, Thériault S, Aeschbacher S, Schoen T, Kunz S, von Rotz M, Estis J, Todd J, Risch M, Mueller C, Risch L, Paré G, Conen D.

BACKGROUND: Determinants of cardiomyocyte injury as quantified by high-sensitivity cardiac troponin I (cTnI) in young and healthy individuals, and sex-specific 99th percentiles are largely unknown.

METHODS: Our study included 2077 adults from the general population aged 25-41 years without cardiovascular disease. cTnI was measured using a high-sensitivity assay. We performed stepwise backward linear regression analyses to identify variables independently associated with hs-cTnI levels, and calculated narrow-sense heritability from 1638-genotyped participants.

RESULTS: Median age was 37 years. cTnI was quantifiable in all but 11 participants (99.5 %). Median (interquartile range) cTnI was significantly higher in men than in women [0.99 (0.71; 1.65) versus 0.47 (0.33; 0.71) ng/L, $p < 0.0001$]. The 99th percentile of cTnI was 15.79 ng/L in men and 5.11 ng/L in women. Out of 46 variables, 22 independent determinants for cTnI were identified. The strongest associations were observed with sex, age, systolic blood pressure, heart rate, left ventricular mass, N-terminal pro B-type natriuretic peptide, and creatine kinase (all $p < 0.0001$). The final model explained 36 % of the overall cTnI variability. Heritability of cTnI was estimated to be 29 % ($p = 0.005$), but became non-significant when the residuals of the multivariable model were used for analysis (5 %, $p = 0.36$).

CONCLUSIONS: Sex, age, and systolic blood pressure belong to the strongest determinants of hs-cTnI in healthy adults. The 99th percentile was three times higher in men compared to women. Hence, sex-specific cut-off values may be preferable when applying hs-cTnI for screening purposes. Our results may also improve the interpretation of cTn levels in daily clinical practice.

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PMID: 27535138 [Indexed for MEDLINE]

Ann Vasc Surg. 2017 Feb;39:173-181.

Carotid Plaque Morphology in Asymptomatic Patients with and without Metabolic Syndrome.

Cury MV, Presti C, Bonadiman SS, Casella IB, Benabou JE, da Silva ES, de Luccia N, Puech-Leão P.

BACKGROUND: The aim of this study was to determine the impact of metabolic syndrome (MetS) on the morphology of carotid plaques, as evaluated using duplex ultrasound (DUS) with computer-assisted analysis.

METHODS: In this cross-sectional observational study, we analyzed 148 carotid artery plaques in asymptomatic patients. Data were obtained via clinical and laboratory examinations, and DUS was performed by a single operator. All plaques were scanned in a longitudinal fashion, and the best segment was selected, recorded, and evaluated using dedicated software. The main software-based analyses included gray-scale median (GSM) measurements and carotid plaque morphology histograms.

RESULTS: MetS was identified in 51.8% of patients. Comparisons of patients with MetS and patients without MetS indicated that the former patients used more classes of antihypertensive drugs (2.49 vs. 1.93; P = 0.004) and were treated with statins for a longer period (71.08 vs. 49.17 months; P = 0.003). Most patients of both types exhibited moderate carotid artery stenosis ranging from 50% to 69% (n = 62; 37.3%), and MetS was not associated with an increased prevalence of severe carotid artery stenosis. The mean GSM was greater in the MetS group than in the non-MetS group (74.18 vs. 61.63; P = 0.012). The histogram analysis revealed that there were lower quantities of blood and fat (2.91 vs. 3.88; P = 0.006; 10.21 vs. 15.08; P = 0.004, respectively) and more fibrous tissue (19.93 vs. 14.55; P = 0.015) in the carotid plaques of patients with MetS than in the carotid plaques of patients without MetS.

CONCLUSIONS: The present study demonstrated that MetS did not affect the stenosis grade or did it lead to unstable carotid plaques.

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PMID: 27522984 [Indexed for MEDLINE]

Curr Cardiol Rev. 2017;13(1):56-62.

Helminth Infections and Cardiovascular Diseases: Toxocara Species is Contributing to the Disease.

Zibaei M.

Toxocariasis is the clinical term used to describe human infection with either the dog ascarid Toxocara canis or the feline ascarid Toxocara cati. As with other helminths zoonoses, the infective larvae of these Toxocara species cannot mature into adults in the human host. Instead, the worms wander through organs and tissues, mainly the liver, lungs, myocardium, kidney and central nervous system, in a vain attempt to find that, which they need to mature into adults. The migration of these immature nematode larvae causes local and systemic inflammation, resulting in the "larva migrans" syndrome. The clinical manifestations of toxocariasis are divided into visceral larva migrans, ocular larva migrans and neurotoxocariasis. Subclinical infection is often referred to as covert toxocariasis. One of the primary causes of death all around the world is cardiovascular disease that accounted for up to 30 percent of all-cause mortality.

Cardiovascular disease and more precisely atherosclerotic cardiovascular disease, is predicted to remain the single leading cause of death (23.3 million deaths by 2030). A-quarter of people presenting the disease does not show any of the known cardiovascular risk factors. Therefore, there is considerable interest in looking for novel components affecting cardiovascular health, especially for those that could improve global cardiovascular risk prediction. This review endeavours to summarize the clinical aspects, new diagnostic and therapeutic perspectives of toxocaral disease with cardiovascular manifestations.

PMID: 27492228 [Indexed for MEDLINE]

Diabetes Metab Syndr. 2017 Jan - Mar;11(1):37-41.

Association of obesity with hypertension and dyslipidemia in type 2 diabetes mellitus subjects.

Anari R, Amani R, Latifi SM, Veissi M, Shahbazian H.

AIM: Obesity and diabetes are contributed to cardiovascular disease risk. The current study was performed to evaluate the association of central and general obesity and cardio-metabolic risk factors, including dyslipidemia and hypertension in T2DM patients.

METHODS: This was a cross-sectional study in T2DM adults. Body mass index (BMI) was used to identify general obesity and waist circumference (WC) was measured to define abdominal obesity (based on ATP III). Biochemical analyses, and anthropometric and blood pressure measurements were done for all participants.

RESULTS: Participants with central obesity showed significantly higher systolic (132.5mmHg vs. 125.4mmHg, p=0.024) and diastolic blood pressures (84.9mmHg vs. 80mmHg, p=0.007) than participants without obesity. Dyslipidemia was more prevalent in all participants either by BMI (98.3% vs. 97%, 95% CI: 0.18-17.53) or by WC (97.2% vs. 98%, 95% CI: 0.07-7.19). Abdominal adiposity in diabetic subjects showed significant reverse association with high level of physical activity (OR=0.22, 95% CI: 0.06-0.85). Hypertriglyceridemia rate was increased with both central (OR=2.11; p=0.040) and general obesity (OR=2.68; p=0.021). After adjustment for energy intake and age, females had higher risk of general (OR=4.57, 95% CI=1.88-11.11) and central obesity (OR=7.93, 95% CI=3.48-18.08).

CONCLUSIONS: Females were more susceptible to obesity. Hypertension was associated with both obesity measures. Dyslipidemia, except for hypertriglyceridemia, was correlated to neither abdominal nor general obesity.

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PMID: 27477531 [Indexed for MEDLINE]

Spinal Cord. 2017 Jan;55(1):87-93.

Cardiovascular disease risk in people with spinal cord injury: is there a possible association between reduced lung function and increased risk of diabetes and hypertension?

Köseoğlu BF, Safer VB, Öken Ö, Akselim S.

STUDY DESIGN: Retrospective, descriptive study of medical files 253 patients with chronic traumatic spinal cord injury (SCI).

OBJECTIVES: To determine the frequency of cardiovascular disease (CVD) risk factors in SCI people, to estimate CVD risk in this population according to the Framingham Risk Score (FRS) and to determine whether reduced lung function parameters are significant predictors of diabetes mellitus (DM) and hypertension.

SETTING: Academic Rehabilitation Hospital.

METHODS: Demographic and clinical records of the patients and lung function parameters were obtained.

RESULTS: The FRS could not be calculated in 26 (10.3%) patients because this tool is designed for adults aged 20 years and older. According to the FRS guideline, ~6.7% of the SCI patients had high risk, 5.9% of them had intermediate risk and 77.1% of the study group had low risk for CVD. Regression analysis showed that impaired lung function parameters (FEV1, FVC and MVV) were significant predictors for the future development of hypertension (odds ratio (OR): 0.483 (0.258-0.903 95% confidence interval (CI)), OR: 0.549 (0.319-0.946 95% CI) and OR: 0.981 (0.965-0.998 95% CI), respectively) and DM (OR: 0.335 (0.140-0.801 95% CI), OR: 0.391 (0.183-0.839 95% CI) and OR: 0.970 (0.947-0.993 95% CI), respectively) in the SCI population.

CONCLUSION: This study showed that there might be a significant relationship between reduced lung function and the risk of DM and hypertension in people with SCI. Therefore, systematic measurement of these parameters should be performed in the routine clinical follow-up of SCI patients. Once reduced lung parameters are determined, the higher risk for developing hypertension and DM should be considered.

DOI: 10.1038/sc.2016.101
PMID: 27377303 [Indexed for MEDLINE]

Arch Physiol Biochem. 2017 Feb;123(1):16-22

Usefulness of the LDL-C/apoB ratio in the overall evaluation of atherogenicity of lipid profile.

Kaneva AM, Potolitsyna NN, Bojko ER.

CONTEXT: The ratio of low-density lipoprotein cholesterol to apolipoprotein-B (LDL-C/apoB) conventionally represents an alternative index of LDL particle size.
OBJECTIVE: This study was undertaken to determine the importance of LDL-C/apoB ratio in the overall evaluation of atherogenicity of lipid profile.

METHODS: The plasma levels of total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), apolipoprotein (apo) A-I, apoB and apoE were measured in 186 apparently healthy men using enzymatic and immunoturbidimetric methods.

RESULTS: The subjects with low values of the LDL-C/apoB ratio, indicating a predominance of small dense LDL (sd-LDL) particles in plasma, were characterized by higher TG levels and lower apoE levels.

CONCLUSION: Low levels of apoE are most likely a cause of reduced clearance of TG-rich lipoproteins, which promotes the formation of sd-LDL. Determination of the LDL-C/apoB ratio can be used for monitoring qualitative changes in lipid profile, in addition to traditional lipid variables indicating quantitative changes.

DOI: 10.1080/13813455.2016.1195411
PMID: 27347637 [Indexed for MEDLINE]

Clin Chem Lab Med. 2017 Mar 1;55(3):314-321.

Serum uric acid levels and risk of prehypertension: a meta-analysis.

Jiang M, Gong D, Fan Y.

Elevated serum uric acid (SUA) levels may increase the risk of prehypertension. However, the findings from these studies remain conflicting. The objective of this study was to determine the relationship between SUA levels and risk of prehypertension by conducting a meta-analysis. We conducted a comprehensive literature search of PubMed, Embase, China National Knowledge Infrastructure, VIP, and the Wangfang database without language restrictions through May 2015.

Observational studies assessing the relationship between SUA levels and prevalence of prehypertension were included. Pooled adjust odds ratio (OR) and corresponding 95% confidence intervals (CI) of prehypertension were calculated for the highest vs. lowest SUA levels. Prehypertension was defined as systolic blood pressure (BP) ranging from 120 to 139 mmHg or diastolic BP ranging from 80 to 89 mmHg. Eight cross-sectional studies with a total of 21,832 prehypertensive individuals were included. Meta-analysis showed that elevated SUA levels were associated with increased risk of prehypertension (OR: 1.84; 95% CI: 1.42-2.38) comparing the highest vs. lowest level of SUA levels. Subgroup analyses showed that elevated SUA levels significantly increased the risk of prehypertension among men (OR: 1.60; 95% CI: 1.12-2.21) and women (OR: 1.59; 95% CI: 1.17-2.16). Elevated SUA levels are positively associated with the risk of prehypertension in the general population.

However, more well-designed longitudinal studies are needed before a definitive conclusion can be drawn due to the cross-sectional studies included are susceptible to bias.

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Ticagrelor versus Clopidogrel in Symptomatic Peripheral Artery Disease

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Background: Peripheral artery disease is considered to be a manifestation of systemic atherosclerosis with associated adverse cardiovascular and limb events. Data from previous trials have suggested that patients receiving clopidogrel monotherapy had a lower risk of cardiovascular events than those receiving aspirin. We wanted to compare clopidogrel with ticagrelor, a potent antiplatelet agent, in patients with peripheral artery disease.

Methods:In this double-blind, event-driven trial, we randomly assigned 13,885 patients with symptomatic peripheral artery disease to receive monotherapy with ticagrelor (90 mg twice daily) or clopidogrel (75 mg once daily). Patients were eligible if they had an ankle–brachial index (ABI) of 0.80 or less or had undergone previous revascularization of the lower limbs. The primary efficacy end point was a composite of adjudicated cardiovascular death, myocardial infarction, or ischemic stroke. The primary safety end point was major bleeding. The median follow-up was 30 months.

Results: The median age of the patients was 66 years, and 72% were men; 43% were enrolled on the basis of the ABI and 57% on the basis of previous revascularization. The mean baseline ABI in all patients was 0.71, 76.6% of the patients had claudication, and 4.6% had critical limb ischemia. The primary efficacy end point occurred in 751 of 6930 patients (10.8%) receiving ticagrelor and in 740 of 6955 (10.6%) receiving clopidogrel (hazard ratio, 1.02; 95% confidence interval [CI], 0.92 to 1.13; P=0.65). In each group, acute limb ischemia occurred in 1.7% of the patients (hazard ratio, 1.03; 95% CI, 0.79 to 1.33; P=0.85) and major bleeding in 1.6% (hazard ratio, 1.10; 95% CI, 0.84 to 1.43; P=0.49).

Conclusions: In patients with symptomatic peripheral artery disease, ticagrelor was not shown to be superior to clopidogrel for the reduction of cardiovascular events. Major bleeding occurred at similar rates among the patients in the two trial groups.

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A Highly Durable RNAi Therapeutic Inhibitor of PCSK9

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Background: Inclisiran (ALN-PCSsc) is a long-acting RNA interference (RNAi) therapeutic agent that inhibits the synthesis of proprotein convertase subtilisin–kexin type 9 (PCSK9), a target for the lowering of low-density lipoprotein (LDL) cholesterol.

Methods: In this phase 1 trial, we randomly assigned healthy volunteers with an LDL cholesterol level of at least 100 mg per deciliter in a 3:1 ratio to receive a subcutaneous injection of inclisiran or placebo in either a single-ascending-dose phase (at a dose of 25, 100, 300, 500, or 800 mg) or a multiple-dose phase (125 mg weekly for four doses, 250 mg every other week for two doses, or 300 or 500 mg monthly for two doses, with or without concurrent statin therapy); each dose cohort included four to eight participants. Safety, the side-effect profile, and pharmacodynamic measures (PCSK9 level, LDL cholesterol level, and exploratory lipid variables) were evaluated.

Results: The most common adverse events were cough, musculoskeletal pain, nasopharyngitis, headache, back pain, and diarrhea. All the adverse events were mild or moderate in severity. There were no serious adverse events or discontinuations due to adverse events. There was one grade 3 elevation in the γ-glutamyltransferase level, which was considered by the investigator to be related to statin therapy. In the single-dose phase, inclisiran doses of 300 mg or more reduced the PCSK9 level (up to a least-squares mean reduction of 74.5% from baseline to day 84), and doses of 100 mg or more reduced the LDL cholesterol level (up to a least-squares mean reduction of 50.6% from baseline). Reductions in the levels of PCSK9 and LDL cholesterol were maintained at day 180 for doses of 300 mg or more. All multiple-dose regimens reduced the levels of PCSK9 (up to a least-squares mean reduction of 83.8% from baseline to day 84) and LDL cholesterol (up to a least-squares mean reduction of 59.7% from baseline to day 84).

Conclusions: In this phase 1 trial, no serious adverse events were observed with inclisiran. Doses of 300 mg or more (in single or multiple doses) significantly reduced levels of PCSK9 and LDL cholesterol for at least 6 months.

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Thromboprophylaxis after Knee Arthroscopy and Lower-Leg Casting

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Background-The use of thromboprophylaxis to prevent clinically apparent venous thromboembolism after knee arthroscopy or casting of the lower leg is disputed. We compared the incidence of symptomatic venous thromboembolism after these procedures between patients who received anticoagulant therapy and those who received no anticoagulant therapy.

Methods-We conducted two parallel, pragmatic, multicenter, randomized, controlled, open-label trials with blinded outcome evaluation: the POT-KAST trial, which included patients undergoing knee arthroscopy, and the POT-CAST trial, which included patients treated with casting of the lower leg. Patients were assigned to receive either a prophylactic dose of low-molecular-weight heparin (for the 8 days after arthroscopy in the POT-KAST trial or during the full period of immobilization due to casting in the POT-CAST trial) or no anticoagulant therapy. The primary outcomes were the cumulative incidences of symptomatic venous thromboembolism and major bleeding within 3 months after the procedure.

Results-In the POT-KAST trial, 1543 patients underwent randomization, of whom 1451 were included in the intention-to-treat population. Venous thromboembolism occurred in 5 of the 731 patients (0.7%) in the treatment group and in 3 of the 720 patients (0.4%) in the control group (relative risk, 1.6; 95% confidence interval [CI], 0.4 to 6.8; absolute difference in risk, 0.3 percentage points; 95% CI, −0.6 to 1.2). Major bleeding occurred in 1 patient (0.1%) in the treatment group and in 1 (0.1%) in the control group (absolute difference in risk, 0 percentage points; 95% CI, −0.6 to 0.7). In the POT-CAST trial, 1519 patients underwent randomization, of whom 1435 were included in the intention-to-treat population. Venous thromboembolism occurred in 10 of the 719 patients (1.4%) in the treatment group and in 13 of the 716 patients (1.8%) in the control group (relative risk, 0.8; 95% CI, 0.3 to 1.7; absolute difference in risk, −0.4 percentage points; 95% CI, −1.8 to 1.0). No major bleeding events occurred. In both trials, the most common adverse event was infection.

Conclusions-The results of our trials showed that prophylaxis with low-molecular-weight heparin for the 8 days after knee arthroscopy or during the full period of immobilization due to casting was not effective for the prevention of symptomatic venous thromboembolism

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Bariatric Surgery versus Intensive Medical Therapy for Diabetes — 5-Year Outcomes

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Background Long-term results from randomized, controlled trials that compare medical therapy with surgical therapy in patients with type 2 diabetes are limited.

Methods We assessed outcomes 5 years after 150 patients who had type 2 diabetes and a body-mass index (BMI; the weight in kilograms divided by the square of the height in meters) of 27 to 43 were randomly assigned to receive intensive medical therapy alone or intensive medical therapy plus Roux-en-Y gastric bypass or sleeve gastrectomy. The primary outcome was a glycated hemoglobin level of 6.0% or less with or without the use of diabetes medications.

Results Of the 150 patients who underwent randomization, 1 patient died during the 5-year follow-up period; 134 of the remaining 149 patients (90%) completed 5 years of follow-up. At baseline, the mean (±SD) age of the 134 patients was 49±8 years, 66% were women, the mean glycated hemoglobin level was 9.2±1.5%, and the mean BMI was 37±3.5. At 5 years, the criterion for the primary end point was met by 2 of 38 patients (5%) who received medical therapy alone, as compared with 14 of 49 patients (29%) who underwent gastric bypass (unadjusted P=0.01, adjusted P=0.03, P=0.08 in the intention-to-treat analysis) and 11 of 47 patients (23%) who underwent sleeve gastrectomy (unadjusted P=0.03, adjusted P=0.07, P=0.17 in the intention-to-treat analysis). Patients who underwent surgical procedures had a greater mean percentage reduction from baseline in glycated hemoglobin level than did patients who received medical therapy alone (2.1% vs. 0.3%, P=0.003). At 5 years, changes from baseline observed in the gastric-bypass and sleeve-gastrectomy groups were superior to the changes seen in the medical-therapy group with respect to body weight (−23%, −19%, and −5% in the gastric-bypass, sleeve-gastrectomy, and medical-therapy groups, respectively), triglyceride level (−40%, −29%, and −8%), high-density lipoprotein cholesterol level (32%, 30%, and 7%), use of insulin (−35%, −34%, and −13%), and quality-of-life measures (general health score increases of 17, 16, and 0.3; scores on the RAND 36-Item Health Survey ranged from 0 to 100, with higher scores indicating better health) (P<0.05 for all comparisons). No major late surgical complications were reported except for one reoperation.

Conclusions Five-year outcome data showed that, among patients with type 2 diabetes and a BMI of 27 to 43, bariatric surgery plus intensive medical therapy was more effective than intensive medical therapy alone in decreasing, or in some cases resolving, hyperglycemia

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Rivaroxaban or Aspirin for Extended Treatment of Venous Thromboembolism

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Background : Although many patients with venous thromboembolism require extended treatment, it is uncertain whether it is better to use full- or lower-intensity anticoagulation therapy or aspirin.

Methods In this randomized, double-blind, phase 3 study, we assigned 3396 patients with venous thromboembolism to receive either once-daily rivaroxaban (at doses of 20 mg or 10 mg) or 100 mg of aspirin. All the study patients had completed 6 to 12 months of anticoagulation therapy and were in equipoise regarding the need for continued anticoagulation. Study drugs were administered for up to 12 months. The primary efficacy outcome was symptomatic recurrent fatal or nonfatal venous thromboembolism, and the principal safety outcome was major bleeding.

Results A total of 3365 patients were included in the intention-to-treat analyses (median treatment duration, 351 days). The primary efficacy outcome occurred in 17 of 1107 patients (1.5%) receiving 20 mg of rivaroxaban and in 13 of 1127 patients (1.2%) receiving 10 mg of rivaroxaban, as compared with 50 of 1131 patients (4.4%) receiving aspirin (hazard ratio for 20 mg of rivaroxaban vs. aspirin, 0.34; 95% confidence interval [CI], 0.20 to 0.59; hazard ratio for 10 mg of rivaroxaban vs. aspirin, 0.26; 95% CI, 0.14 to 0.47; P<0.001 for both comparisons). Rates of major bleeding were 0.5% in the group receiving 20 mg of rivaroxaban, 0.4% in the group receiving 10 mg of rivaroxaban, and 0.3% in the aspirin group; the rates of clinically relevant nonmajor bleeding were 2.7%, 2.0%, and 1.8%, respectively. The incidence of adverse events was similar in all three groups.

Conclusions Among patients with venous thromboembolism in equipoise for continued anticoagulation, the risk of a recurrent event was significantly lower with rivaroxaban at either a treatment dose (20 mg) or a prophylactic dose (10 mg) than with aspirin, without a significant increase in bleeding rates.

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Quarter-dose quadruple combination therapy for initial treatment of hypertension: placebo-controlled, crossover, randomised trial and systematic review

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Background Globally, most patients with hypertension are treated with monotherapy, and control rates are poor because monotherapy only reduces blood pressure by around 9/5 mm Hg on average. There is a pressing need for blood pressure-control strategies with improved efficacy and tolerability. We aimed to assess whether ultra-low-dose combination therapy could meet these needs.

Methods We did a randomised, placebo-controlled, double-blind, crossover trial of a quadpill—a single capsule containing four blood pressure-lowering drugs each at quarter-dose (irbesartan 37·5 mg, amlodipine 1·25 mg, hydrochlorothiazide 6·25 mg, and atenolol 12·5 mg). Participants with untreated hypertension were enrolled from four centres in the community of western Sydney, NSW, Australia, mainly by general practitioners. Participants were randomly allocated by computer to either the quadpill or matching placebo for 4 weeks; this treatment was followed by a 2-week washout, then the other study treatment was administered for 4 weeks. Study staff and participants were unaware of treatment allocations, and masking was achieved by use of identical opaque capsules. The primary outcome was placebo-corrected 24-h systolic ambulatory blood pressure reduction after 4 weeks and analysis was by intention to treat. We also did a systematic review of trials evaluating the efficacy and safety of quarter-standard-dose blood pressure-lowering therapy against placebo. This trial is registered with the Australian New Zealand Clinical Trials Registry, number ACTRN12614001057673. The trial ended after 1 year and this report presents the final analysis.

Findings Between November, 2014, and December, 2015, 55 patients were screened for our randomised trial, of whom 21 underwent randomisation. Mean age of participants was 58 years (SD 11) and mean baseline office and 24-h systolic and diastolic blood pressure levels were 154 (14)/90 (11) mm Hg and 140 (9)/87 (8) mm Hg, respectively. One individual declined participation after randomisation and two patients dropped out for administrative reasons. The placebo-corrected reduction in systolic 24-h blood pressure with the quadpill was 19 mm Hg (95% CI 14–23), and office blood pressure was reduced by 22/13 mm Hg ($p<0·0001$). During quadpill treatment, 18 (100%) of 18 participants achieved office blood pressure less than 140/90 mm Hg, compared with six (33%) of 18 during placebo treatment ($p=0·0013$). There were no serious adverse events and all patients reported that the quadpill was easy to swallow. Our systematic review identified 36 trials (n=4721 participants) of one drug at quarter-dose and six trials (n=312) of two drugs at quarter-dose, against

placebo. The pooled placebo-corrected blood pressure-lowering effects were 5/2 mm Hg and 7/5 mm Hg, respectively (both p<0·0001), and there were no side-effects from either regimen.

Interpretation The findings of our small trial in the context of previous randomised evidence suggest that the benefits of quarter-dose therapy could be additive across classes and might confer a clinically important reduction in blood pressure. Further examination of the quadpill concept is needed to investigate effectiveness against usual treatment options and longer term tolerability

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Socioeconomic status and the 25 × 25 risk factors as determinants of premature mortality: a multicohort study and meta-analysis of 1·7 million men and women

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Background In 2011, WHO member states signed up to the 25 × 25 initiative, a plan to cut mortality due to non-communicable diseases by 25% by 2025. However, socioeconomic factors influencing non-communicable diseases have not been included in the plan. In this study, we aimed to compare the contribution of socioeconomic status to mortality and years-of-life-lost with that of the 25 × 25 conventional risk factors.

Methods- We did a multicohort study and meta-analysis with individual-level data from 48 independent prospective cohort studies with information about socioeconomic status, indexed by occupational position, 25 × 25 risk factors (high alcohol intake, physical inactivity, current smoking, hypertension, diabetes, and obesity), and mortality, for a total population of 1 751 479 (54% women) from seven high-income WHO member countries. We estimated the association of socioeconomic status and the 25 × 25 risk factors with all-cause mortality and cause-specific mortality by calculating minimally adjusted and mutually adjusted hazard ratios [HR] and 95% CIs. We also estimated the population attributable fraction and the years of life lost due to suboptimal risk factors.

Findings During 26·6 million person-years at risk (mean follow-up 13·3 years [SD 6·4 years]), 310 277 participants died. HR for the 25 × 25 risk factors and mortality varied between 1·04 (95% CI 0·98–1·11) for obesity in men and 2 ·17 (2·06–2·29) for current smoking in men. Participants with low socioeconomic status had greater mortality compared with those with high socioeconomic status (HR 1·42, 95% CI 1·38–1·45 for men; 1·34, 1·28–1·39 for women); this association remained significant in mutually adjusted models that included the 25 × 25 factors (HR 1·26, 1·21–1·32, men and women combined). The population attributable fraction was highest for smoking, followed by physical inactivity then socioeconomic status. Low socioeconomic status was associated with a 2·1-year reduction in life expectancy between ages 40 and 85 years, the corresponding years-of-life-lost were 0·5 years for high alcohol intake, 0·7 years for obesity, 3·9 years for diabetes, 1·6 years for hypertension, 2·4 years for physical inactivity, and 4·8 years for current smoking.

Interpretation Socioeconomic circumstances, in addition to the 25 × 25 factors, should be targeted by local and global health strategies and health risk surveillance to reduce mortality.

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Efficacy and effectiveness of screen and treat policies in prevention of type 2 diabetes: systematic review and meta-analysis of screening tests and interventions

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Objectives To assess diagnostic accuracy of screening tests for pre-diabetes and efficacy of interventions (lifestyle or metformin) in preventing onset of type 2 diabetes in people with pre-diabetes.

Design Systematic review and meta-analysis.

Data sources and method Medline, PreMedline, and Embase. Two meta analyses were performed, one summarising accuracy of screening tests (with the oral glucose tolerance test as the standard) for identification of pre-diabetes, and the other assessing relative risk of progression to type 2 diabetes after either lifestyle intervention or treatment with metformin.

Eligibility criteria Empirical studies evaluating accuracy of tests for identification of pre-diabetes. Interventions (randomised trials and interventional studies) with a control group in people identified through screening. No language restrictions.

Results 2874 titles were scanned and 148 papers (covering 138 studies) reviewed in full. The final analysis included 49 studies of screening tests (five of which were prevalence studies) and 50 intervention trials. HbA1c had a mean sensitivity of 0.49 (95% confidence interval 0.40 to 0.58) and specificity of 0.79 (0.73 to 0.84), for identification of pre-diabetes, though different studies used different cut-off values. Fasting plasma glucose had a mean sensitivity of 0.25 (0.19 to 0.32) and specificity of 0.94 (0.92 to 0.96). Different measures of glycaemic abnormality identified different subpopulations (for example, 47% of people with abnormal HbA1c had no other glycaemic abnormality). Lifestyle interventions were associated with a 36% (28% to 43%) reduction in relative risk of type 2 diabetes over six months to six years, attenuating to 20% (8% to 31%) at follow-up in the period after the trails.

Conclusions HbA1c is neither sensitive nor specific for detecting pre-diabetes; fasting glucose is specific but not sensitive. Interventions in people classified through screening as having pre-diabetes have some efficacy in preventing or delaying onset of type 2 diabetes in trial populations. As screening is inaccurate, many people will receives an incorrect diagnosis and be referred on for interventions while others will be falsely reassured and not offered the intervention. These findings suggest that “screen and treat” policies alone are unlikely to have substantial impact on the worsening epidemic of type 2 diabetes.

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Renin angiotensin system inhibitors for patients with stable coronary artery disease without heart failure: systematic review and meta-analysis of randomized trials

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Objective To critically evaluate the efficacy of renin angiotensin system inhibitors (RASi) in patients with coronary artery disease without heart failure, compared with active controls or placebo.

Design Meta-analysis of randomized trials.

Eligibility criteria for selecting studies Randomized trials of RASi versus placebo or active controls in patients with stable coronary artery disease without heart failure (defined as left ventricular ejection fraction ≥40% or without clinical heart failure). Each trial had to enroll at least 100 patients with coronary artery disease without heart failure, with at least one year's follow-up. Studies were excluded if they were redacted or compared use of angiotensin converting enzyme inhibitors with angiotensin receptor blockers. Outcomes were death, cardiovascular death, myocardial infarction, angina, stroke, heart failure, revascularization, incident diabetes, and drug withdrawal due to adverse effects.

Results 24 trials with 198 275 patient years of follow-up were included. RASi reduced the risk of all cause mortality (rate ratio 0.84, 95% confidence interval 0.72 to 0.98), cardiovascular mortality (0.74, 0.59 to 0.94), myocardial infarction (0.82, 0.76 to 0.88), stroke (0.79, 0.70 to 0.89), angina, heart failure, and revascularization when compared with placebo but not when compared with active controls (all cause mortality, 1.05, 0.94 to 1.17; Pinteraction=0.006; cardiovascular mortality, 1.08, 0.93 to 1.25, Pinteraction<0.001; myocardial infarction, 0.99, 0.87 to 1.12, Pinteraction=0.01; stroke, 1.10, 0.93 to 1.31; Pinteraction=0.002). Bayesian meta-regression analysis showed that the effect of RASi when compared with placebo on all cause mortality and cardiovascular mortality was dependent on the control event rate, such that RASi was only beneficial in trials with high control event rates (>14.10 deaths and >7.65 cardiovascular deaths per 1000 patient years) but not in those with low control event rates.

Conclusions In patients with stable coronary artery disease without heart failure, RASi reduced cardiovascular events and death only when compared with placebo but not when compared with active controls. Even among placebo controlled trials in this study, the benefit of RASi was mainly seen in trials with higher control event rates but not in those with lower control event rates. Evidence does not support a preferred status of RASi over other active controls.

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Testosterone Treatment and Coronary Artery Plaque Volume in Older Men With Low Testosterone

Matthew J. Budoff; Susan S. Ellenberg; Cora E. Lewis et al.

Importance Recent studies have yielded conflicting results as to whether testosterone treatment increases cardiovascular risk.

Objective To test the hypothesis that testosterone treatment of older men with low testosterone slows progression of noncalcified coronary artery plaque volume.

Design, Setting, and Participants Double-blinded, placebo-controlled trial at 9 academic medical centers in the United States. The participants were 170 of 788 men aged 65 years or older with an average of 2 serum testosterone levels lower than 275 ng/dL (82 men assigned to placebo, 88 to testosterone) and symptoms suggestive of hypogonadism who were enrolled in the Testosterone Trials between June 24, 2010, and June 9, 2014.

Intervention Testosterone gel, with the dose adjusted to maintain the testosterone level in the normal range for young men, or placebo gel for 12 months.

Main Outcomes and Measures The primary outcome was noncalcified coronary artery plaque volume, as determined by coronary computed tomographic angiography. Secondary outcomes included total coronary artery plaque volume and coronary artery calcium score (range of 0 to >400 Agatston units, with higher values indicating more severe atherosclerosis).

Results Of 170 men who were enrolled, 138 (73 receiving testosterone treatment and 65 receiving placebo) completed the study and were available for the primary analysis. Among the 138 men, the mean (SD) age was 71.2 (5.7) years, and 81% were white. At baseline, 70 men (50.7%) had a coronary artery calcification score higher than 300 Agatston units, reflecting severe atherosclerosis. For the primary outcome, testosterone treatment compared with placebo was associated with a significantly greater increase in noncalcified plaque volume from baseline to 12 months (from median values of 204 mm3 to 232 mm3 vs 317 mm3 to 325 mm3, respectively; estimated difference, 41 mm3; 95% CI, 14 to 67 mm3; P = .003). For the secondary outcomes, the median total plaque volume increased from baseline to 12 months from 272 mm3 to 318 mm3 in the testosterone group vs from 499 mm3 to 541 mm3 in the placebo group (estimated difference, 47 mm3; 95% CI, 13 to 80 mm3; P = .006), and the median coronary artery calcification score changed from 255 to 244 Agatston units in the testosterone group vs 494 to 503 Agatston units in the placebo group (estimated difference, −27 Agatston units; 95% CI, −80 to 26 Agatston units). No major adverse cardiovascular events occurred in either group.

Conclusions and Relevance Among older men with symptomatic hypogonadism, treatment with testosterone gel for 1 year compared with placebo was associated with a significantly greater increase in coronary artery noncalcified plaque volume, as measured by coronary computed tomographic angiography. Larger studies are needed to understand the clinical implications of this finding

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Association of Antithrombotic Drug Use With Subdural Hematoma Risk

David Gaist, Luis Alberto García Rodríguez, Maja Hellfritzsch et al.

Importance Incidence of subdural hematoma has been reported to be increasing. To what extent this is related to increasing use of antithrombotic drugs is unknown.

Objectives To estimate the association between use of antithrombotic drugs and subdural hematoma risk and determine trends in subdural hematoma incidence and antithrombotic drug use in the general population.

Design, Setting, and Participants Case-control study of 10 010 patients aged 20 to 89 years with a first-ever subdural hematoma principal discharge diagnosis from 2000 to 2015 matched by age, sex, and calendar year to 400 380 individuals from the general population (controls). Subdural hematoma incidence and antithrombotic drug use was identified using population-based regional data (population: 484 346) and national data (population: 5.2 million) from Denmark. Conditional logistic regression models were used to estimate odds ratios (ORs) that were adjusted for comorbidity, education level, and income level.

Exposures Use of low-dose aspirin, clopidogrel, a vitamin K antagonist (VKA), a direct oral anticoagulant, and combined antithrombotic drug treatment.

Main Outcomes and Measures Association of subdural hematoma with antithrombotic drug use, subdural hematoma incidence rate, and annual prevalence of treatment with antithrombotic drugs.

Results Among 10 010 patients with subdural hematoma (mean age, 69.2 years; 3462 women [34.6%]), 47.3% were taking antithrombotic medications. Current use of low-dose aspirin (cases: 26.7%, controls: 22.4%; adjusted OR, 1.24 [95% CI, 1.15-1.33]), clopidogrel (cases: 5.0%, controls: 2.2%; adjusted OR, 1.87 [95% CI, 1.57-2.24]), a direct oral anticoagulant (cases: 1.0%, controls: 0.6%; adjusted OR, 1.73 [95% CI, 1.31-2.28]), and a VKA (cases: 14.3%, controls: 4.9%; adjusted OR, 3.69 [95% CI, 3.38-4.03]) were associated with higher risk of subdural hematoma. The risk of subdural hematoma was highest when a VKA was used concurrently with an antiplatelet drug (low-dose aspirin and a VKA: 3.6% of cases and 1.1% of controls; adjusted OR, 4.00 [95% CI, 3.40-4.70]; clopidogrel and a VKA: 0.3% of cases and 0.04% of controls; adjusted OR, 7.93 [95% CI, 4.49-14.02]). The prevalence of antithrombotic drug use increased from 31.0 per 1000 individuals from the general population in 2000 to 76.9 per 1000 individuals in 2015 ($P < .001$ for trend). The overall subdural hematoma incidence rate increased from 10.9 per 100 000 person-years in 2000 to 19.0 per 100 000 person-years in 2015 ($P < .001$ for trend). The largest increase was among older patients (>75 years; $n = 4441$) who experienced an increase from 55.1 per 100 000 person-years to 99.7 per 100 000 person-years ($P < .001$ for trend).

Conclusions and Relevance In Denmark, antithrombotic drug use was associated with higher risk of subdural hematoma; and the highest odds of subdural hematoma was associated with combined use of a VKA and an antiplatelet drug. The increased incidence of subdural hematoma from 2000 to 2015 appears to be associated with the increased use of antithrombotic drugs, particularly use of a VKA among older patients

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Association Between Dietary Factors and Mortality From Heart Disease, Stroke, and Type 2 Diabetes in the United States

Renata Micha, Jose L. Peñalvo, Frederick Cudhea et al.

Importance In the United States, national associations of individual dietary factors with specific cardiometabolic diseases are not well established.

Objective To estimate associations of intake of 10 specific dietary factors with mortality due to heart disease, stroke, and type 2 diabetes (cardiometabolic mortality) among US adults.

Design, Setting, and Participants A comparative risk assessment model incorporated data and corresponding uncertainty on population demographics and dietary habits from National Health and Nutrition Examination Surveys (1999-2002: n = 8104; 2009-2012: n = 8516); estimated associations of diet and disease from meta-analyses of prospective studies and clinical trials with validity analyses to assess potential bias; and estimated disease-specific national mortality from the National Center for Health Statistics.

Exposures Consumption of 10 foods/nutrients associated with cardiometabolic diseases: fruits, vegetables, nuts/seeds, whole grains, unprocessed red meats, processed meats, sugar-sweetened beverages (SSBs), polyunsaturated fats, seafood omega-3 fats, and sodium.

Main Outcomes and Measures Estimated absolute and percentage mortality due to heart disease, stroke, and type 2 diabetes in 2012. Disease-specific and demographic-specific (age, sex, race, and education) mortality and trends between 2002 and 2012 were also evaluated.

Results In 2012, 702 308 cardiometabolic deaths occurred in US adults, including 506 100 from heart disease (371 266 coronary heart disease, 35 019 hypertensive heart disease, and 99 815 other cardiovascular disease), 128 294 from stroke (16 125 ischemic, 32 591 hemorrhagic, and 79 578 other), and 67 914 from type 2 diabetes. Of these, an estimated 318 656 (95% uncertainty interval [UI], 306 064-329 755; 45.4%) cardiometabolic deaths per year were associated with suboptimal intakes—48.6% (95% UI, 46.2%-50.9%) of cardiometabolic deaths in men and 41.8% (95% UI, 39.3%-44.2%) in women; 64.2% (95% UI, 60.6%-67.9%) at younger ages (25-34 years) and 35.7% (95% UI, 33.1%-38.1%) at older ages (≥75 years); 53.1% (95% UI, 51.6%-54.8%) among blacks, 50.0% (95% UI, 48.2%-51.8%) among Hispanics, and 42.8% (95% UI, 40.9%-44.5%) among whites; and 46.8% (95% UI, 44.9%-48.7%) among lower-, 45.7% (95% UI, 44.2%-47.4%) among medium-, and 39.1% (95% UI, 37.2%-41.2%) among higher-educated individuals. The largest numbers of estimated diet-related cardiometabolic deaths were related to high sodium (66 508 deaths in 2012; 9.5% of all cardiometabolic deaths), low nuts/seeds (59 374; 8.5%), high processed meats (57 766; 8.2%), low seafood omega-3 fats (54 626; 7.8%), low vegetables (53 410; 7.6%), low fruits (52 547; 7.5%), and high SSBs (51 694; 7.4%). Between 2002 and 2012, population-adjusted US cardiometabolic deaths per year decreased by 26.5%. The greatest decline was associated with insufficient polyunsaturated

fats (−20.8% relative change [95% UI, −18.5% to −22.8%]), nuts/seeds (−18.0% [95% UI, −14.6% to −21.0%]), and excess SSBs (−14.5% [95% UI, −12.0% to −16.9%]). The greatest increase was associated with unprocessed red meats (+14.4% [95% UI, 9.1%-19.5%]).

Conclusions and Relevance Dietary factors were estimated to be associated with a substantial proportion of deaths from heart disease, stroke, and type 2 diabetes. These results should help identify priorities, guide public health planning, and inform strategies to alter dietary habits and improve health.

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Association of Rare and Common Variation in the Lipoprotein Lipase Gene With Coronary Artery Disease

Amit V. Khera, MD; Hong-Hee Won, PhD; Gina M. Peloso, PhD; et al.

Importance The activity of lipoprotein lipase (LPL) is the rate-determining step in clearing triglyceride-rich lipoproteins from the circulation. Mutations that damage the LPL gene (LPL) lead to lifelong deficiency in enzymatic activity and can provide insight into the relationship of LPL to human disease.

Objective To determine whether rare and/or common variants in LPL are associated with early-onset coronary artery disease (CAD).

Design, Setting, and Participants In a cross-sectional study, LPL was sequenced in 10 CAD case-control cohorts of the multinational Myocardial Infarction Genetics Consortium and a nested CAD case-control cohort of the Geisinger Health System DiscovEHR cohort between 2010 and 2015. Common variants were genotyped in up to 305 699 individuals of the Global Lipids Genetics Consortium and up to 120 600 individuals of the CARDIoGRAM Exome Consortium between 2012 and 2014. Study-specific estimates were pooled via meta-analysis.

Exposures Rare damaging mutations in LPL included loss-of-function variants and missense variants annotated as pathogenic in a human genetics database or predicted to be damaging by computer prediction algorithms trained to identify mutations that impair protein function. Common variants in the LPL gene region included those independently associated with circulating triglyceride levels.

Main Outcomes and Measures Circulating lipid levels and CAD.

Results Among 46 891 individuals with LPL gene sequencing data available, the mean (SD) age was 50 (12.6) years and 51% were female. A total of 188 participants (0.40%; 95% CI, 0.35%-0.46%) carried a damaging mutation in LPL, including 105 of 32 646 control participants (0.32%) and 83 of 14 245 participants with early-onset CAD (0.58%). Compared with 46 703 noncarriers, the 188 heterozygous carriers of an LPL damaging mutation displayed higher plasma triglyceride levels (19.6 mg/dL; 95% CI, 4.6-34.6 mg/dL) and higher odds of CAD (odds ratio = 1.84; 95% CI, 1.35-2.51; $P < .001$). An analysis of 6 common LPL variants resulted in an odds ratio for CAD of 1.51 (95% CI, 1.39-1.64; $P = 1.1 \times 10{-}22$) per 1-SD increase in triglycerides.

Conclusions and Relevance The presence of rare damaging mutations in LPL was significantly associated with higher triglyceride levels and presence of coronary artery disease. However, further research is needed to assess whether there are causal mechanisms by which heterozygous lipoprotein lipase deficiency could lead to coronary artery disease.

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Association of Preceding Antithrombotic Treatment With Acute Ischemic Stroke Severity and In-Hospital Outcomes Among Patients With Atrial Fibrillation

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Importance Antithrombotic therapies are known to prevent stroke for patients with atrial fibrillation (AF) but are often underused in community practice.

Objectives To examine the prevalence of patients with acute ischemic stroke with known history of AF who were not receiving guideline-recommended antithrombotic treatment before stroke and to determine the association of preceding antithrombotic therapy with stroke severity and in-hospital outcomes.

Design, Setting, and Participants Retrospective observational study of 94 474 patients with acute ischemic stroke and known history of AF admitted from October 2012 through March 2015 to 1622 hospitals participating in the Get With the Guidelines–Stroke program.

Exposures Antithrombotic therapy before stroke.

Main Outcomes and Measures Stroke severity as measured by the National Institutes of Health Stroke Scale (NIHSS; range of 0-42, with a higher score indicating greater stroke severity and a score ≥16 indicating moderate or severe stroke), and in-hospital mortality.

Results Of 94 474 patients (mean [SD] age, 79.9 [11.0] years; 57.0% women), 7176 (7.6%) were receiving therapeutic warfarin (international normalized ratio [INR] ≥2) and 8290 (8.8%) were receiving non–vitamin K antagonist oral anticoagulants (NOACs) preceding the stroke. A total of 79 008 patients (83.6%) were not receiving therapeutic anticoagulation; 12 751 (13.5%) had subtherapeutic warfarin anticoagulation (INR <2) at the time of stroke, 37 674 (39.9%) were receiving antiplatelet therapy only, and 28 583 (30.3%) were not receiving any antithrombotic treatment. Among 91 155 high-risk patients (prestroke CHA2DS2-VASc score ≥2), 76 071 (83.5%) were not receiving therapeutic warfarin or NOACs before stroke. The unadjusted rates of moderate or severe stroke were lower among patients receiving therapeutic warfarin (15.8% [95% CI, 14.8%-16.7%]) and NOACs (17.5% [95% CI, 16.6%-18.4%]) than among those receiving no antithrombotic therapy (27.1% [95% CI, 26.6%-27.7%]), antiplatelet therapy only (24.8% [95% CI, 24.3%-25.3%]), or subtherapeutic warfarin (25.8% [95% CI, 25.0%-26.6%]); unadjusted rates of in-hospital mortality also were lower for those receiving therapeutic warfarin (6.4% [95% CI, 5.8%-7.0%]) and NOACs (6.3% [95% CI, 5.7%-6.8%]) compared with those receiving no antithrombotic therapy (9.3% [95% CI, 8.9%-9.6%]), antiplatelet therapy only (8.1% [95% CI, 7.8%-8.3%]), or subtherapeutic warfarin (8.8% [95% CI, 8.3%-9.3%]). After adjusting for potential confounders, compared with no antithrombotic treatment, preceding use of therapeutic warfarin, NOACs, or antiplatelet therapy was associated with lower odds of moderate or severe stroke (adjusted odds ratio [95% CI], 0.56 [0.51-0.60], 0.65 [0.61-0.71],

and 0.88 [0.84-0.92], respectively) and in-hospital mortality (adjusted odds ratio [95% CI], 0.75 [0.67-0.85], 0.79 [0.72-0.88], and 0.83 [0.78-0.88], respectively).

Conclusions and Relevance Among patients with atrial fibrillation who had experienced an acute ischemic stroke, inadequate therapeutic anticoagulation preceding the stroke was prevalent. Therapeutic anticoagulation was associated with lower odds of moderate or severe stroke and lower odds of in-hospital mortality

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Association Between Dabigatran vs Warfarin and Risk of Osteoporotic Fractures Among Patients With Nonvalvular Atrial Fibrillation

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Importance The risk of osteoporotic fracture with dabigatran use in patients with nonvalvular atrial fibrillation (NVAF) is unknown.

Objective To investigate the risk of osteoporotic fracture with dabigatran vs warfarin in patients with NVAF.

Design, Setting, and Participants Retrospective cohort study using a population-wide database managed by the Hong Kong Hospital Authority. Patients newly diagnosed with NVAF from 2010 through 2014 and prescribed dabigatran or warfarin were matched by propensity score at a 1:2 ratio with follow-up until July 31, 2016.

Exposures Dabigatran or warfarin use during the study period.

Main Outcomes and Measures Risk of osteoporotic hip fracture and vertebral fracture was compared between dabigatran and warfarin users using Poisson regression. The corresponding incidence rate ratio (IRR) and absolute risk difference (ARD) with 95% CIs were calculated.

Results Among 51 496 patients newly diagnosed with NVAF, 8152 new users of dabigatran (n = 3268) and warfarin (n = 4884) were matched by propensity score (50% women; mean [SD] age, 74 [11] years). Osteoporotic fracture developed in 104 (1.3%) patients during follow-up (32 dabigatran users [1.0%]; 72 warfarin users [1.5%]). Results of Poisson regression analysis showed that dabigatran use was associated with a significantly lower risk of osteoporotic fracture compared with warfarin (0.7 vs 1.1 per 100 person-years; ARD per 100 person-years, −0.68 [95% CI, −0.38 to −0.86]; IRR, 0.38 [95% CI, 0.22 to 0.66]). The association with lower risk was statistically significant in patients with a history of falls, fractures, or both (dabigatran vs warfarin, 1.6 vs 3.6 per 100 person-years; ARD per 100 person-years, −3.15 [95% CI, −2.40 to −3.45]; IRR, 0.12 [95% CI, 0.04 to 0.33]), but not in those without a history (0.6 vs 0.7 per 100 person-years; ARD per 100 person-years, −0.04 [95% CI, 0.67 to −0.39]; IRR, 0.95 [95% CI, 0.45 to 1.96]) (P value for interaction, <.001).

Conclusions and Relevance Among adults with NVAF receiving anticoagulation, the use of dabigatran compared with warfarin was associated with a lower risk of osteoporotic fracture. Additional study, perhaps including randomized clinical trials, may be warranted to further understand the relationship between use of dabigatran vs warfarin and risk of fracture.

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Effectiveness and safety of reduced dose non-vitamin K antagonist oral anticoagulants and warfarin in patients with atrial fibrillation: propensity weighted nationwide cohort study

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Objective To examine clinical effectiveness and safety of apixaban 2.5 mg, dabigatran 110 mg, and rivaroxaban 15 mg compared with warfarin among patients with atrial fibrillation who had not previously taken an oral anticoagulant.

Design Propensity weighted (inverse probability of treatment weighted) nationwide cohort study.
Setting Individual linked data from three nationwide registries in Denmark.

Participants Patients with non-valvular atrial fibrillation filling a first prescription for an oral anticoagulant from August 2011 to February 2016. Patients who filled a prescription for a standard dose non-vitamin K antagonist oral anticoagulant (novel oral anticoagulants, NOACs) were excluded. To control for baseline differences in the population, a propensity score for receipt of either of the four treatment alternatives was calculated to apply an inverse probability treatment weight.
Intervention Initiated anticoagulant treatment (dabigatran 110 mg, rivaroxaban 15 mg, apixaban 2.5 mg, and warfarin).
Main outcome measures Patients were followed in the registries from onset of treatment for the primary effectiveness outcome of ischaemic stroke/systemic embolism and for the principal safety outcome of any bleeding events.

Results Among 55 644 patients with atrial fibrillation who met inclusion criteria, the cohort was distributed according to treatment: apixaban n=4400; dabigatran n=8875; rivaroxaban n=3476; warfarin n=38 893. The overall mean age was 73.9 (SD 12.7), ranging from a mean of 71.0 (warfarin) to 83.9 (apixaban). During one year of follow-up, apixaban was associated with higher (weighted) event rate of ischaemic stroke/systemic embolism (4.8%), while dabigatran, rivaroxaban, and warfarin had event rates of 3.3%, 3.5%, and 3.7%, respectively. In the comparison between a non-vitamin K antagonist oral anticoagulant and warfarin in the inverse probability of treatment weighted analyses and investigation of the effectiveness outcome, the hazard ratios were 1.19 (95% confidence interval 0.95 to 1.49) for apixaban, 0.89 (0.77 to 1.03) for dabigatran, and 0.89 (0.69 to 1.16) for rivaroxaban. For the principal safety outcome versus warfarin, the hazard ratios were 0.96 (0.73 to 1.27) for apixaban, 0.80 (0.70 to 0.92) for dabigatran, and 1.06 (0.87 to 1.29) for rivaroxaban.

Conclusion In this propensity weighted nationwide study of reduced dose non-vitamin K antagonist oral anticoagulant regimens, apixaban 2.5 mg twice a day was associated with a trend towards higher rates of ischaemic stroke/systemic embolism compared with warfarin, while rivaroxaban 15 mg once a day and dabigatran 110 mg twice a day showed a trend towards lower thromboembolic rates. The results were not significantly different. Rates of bleeding (the principal safety outcome) were significantly lower for dabigatran, but not significantly different for apixaban and rivaroxaban compared with warfarin.

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Serum creatinine elevation after renin-angiotensin system blockade and long term cardiorenal risks: cohort study

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Objective To examine long term cardiorenal outcomes associated with increased concentrations of reatinine after thestart of angiotensin converting enzyme inhibitor/angiotensin receptor blocker treatment.

DesignPopulation based cohort study using electronic health records from the Clinical Practice Research Datalink and Hospital Episode Statistics.

Setting UK primary care, 1997-2014.

Participants Patients starting treatment with angiotensin converting enzyme inhibitors or angiotensin receptor blockers (n=122 363).

Main outcome measures Poisson regression was used to compare rates of end stage renal disease, myocardial infarction, heart failure, and death among patients with creatinine increases of 30% or more after starting treatment against those without such increases, and for each 10% increase in creatinine. Analyses were adjusted for age, sex, calendar period, socioeconomic status, lifestyle factors, chronic kidney disease, diabetes, cardiovascular comorbidities, and use of other antihypertensive drugs and non-steroidal anti-inflammatory drugs.

Results Among the 2078 (1.7%) patients with creatinine increases of 30% or more, a higher proportion were female, were elderly, had cardiorenal comorbidity, and used non-steroidal anti-inflammatory drugs, loop diuretics, or potassium sparing diuretics. Creatinine increases of 30% or more were associated with an increased adjusted incidence rate ratio for all outcomes, compared with increases of less than 30%: 3.43 (95% confidence interval 2.40 to 4.91) for end stage renal disease, 1.46 (1.16 to 1.84) for myocardial infarction, 1.37 (1.14 to 1.65) for heart failure, and 1.84 (1.65 to 2.05) for death. The detailed categorisation of increases in creatinine concentrations (<10%, 10-19%, 20-29%, 30-39%, and ≥40%) showed a graduated relation for all outcomes (all P values for trends <0.001). Notably, creatinine increases of less than 30% were also associated with increased incidence rate ratios for all outcomes, including death (1.15 (1.09 to 1.22) for increases of 10-19% and 1.35 (1.23 to 1.49) for increases of 20-29%, using <10% as reference). Results were consistent across calendar periods, across subgroups of patients, and among continuing users.

Conclusions Increases in creatinine after the start of angiotensin converting enzyme inhibitor/angiotensin receptor blocker treatment were associated with adverse cardiorenal outcomes in a graduated relation, even below the guideline recommended threshold of a 30% increase for stopping treatment.

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Validating the HERDOO2 rule to guide treatment duration for women with unprovoked venous thrombosis: multinational prospective cohort management study

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Objective To prospectively validate the HERDOO2 rule (Hyperpigmentation, Edema, or Redness in either leg; D-dimer level ≥250 μg/L; Obesity with body mass index ≥30; or Older age, ≥65 years), which states that women with none or one of the criteria can safely discontinue anticoagulants after short term treatment.

Design Prospective cohort management study.

Setting 44 secondary or tertiary care centres in seven countries.

Participants Of 3155 consecutive eligible participants with a first unprovoked venous thromboembolism (VTE, proximal leg deep vein thrombosis or pulmonary embolism) who completed 5-12 months of short term anticoagulant treatment, 370 declined to participate, leaving 2785 enrolled participants. 2.3% were lost to follow-up.

Interventions Women with none or one of the HERDOO2 criteria were classified as at low risk of recurrent VTE and discontinued anticoagulants (intervention arm), whereas anticoagulant management for high risk women (≥2 HERDOO2 criteria) and men was left to the discretion of the clinicians and patients (observation arm).

Main outcom e measure Recurrent symptomatic VTE (independently and blindly adjudicated) over one year of follow-up.

Results Of 1213 women, 631 (51.3%) were classified as low risk and 591 discontinued oral anticoagulant treatment. In the primary analysis, 17 low risk women who discontinued anticoagulants developed recurrent VTE during 564 patient years of follow-up (3.0% per patient year, 95% confidence interval 1.8% to 4.8%). In 323 high risk women and men who discontinued anticoagulants, 25 had VTE during 309 patient years of follow-up (8.1%, 5.2% to 11.9%), whereas in 1802 high risk women and men who continued anticoagulants 28 had recurrent VTE during 1758 patient years of follow-up (1.6%, 1.1% to 2.3%).

Conclusions Women with a first unprovoked VTE event and none or one of the HERDOO2 criteria have a low risk of recurrent VTE and can safely discontinue anticoagulants after completing short term treatment

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Dairy consumption, systolic blood pressure, and risk of hypertension: Mendelian randomization study

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ObjectiveTo examine whether previous observed inverse associations of dairy intake with systolic bloodpressure and risk of hypertension were causal.

DesignMendelian randomization study using the singlenucleotide polymorphism rs4988235 related to lactase persistence as an instrumental variable.

Setting CHARGE (Cohorts for Heart and Aging Research in Genomic Epidemiology) Consortium.

Participants Data from 22 studies with 171 213 participants, and an additional 10 published prospective studies with 26 119 participants included in the observational analysis.

Main outcom e measures The instrumental variable estimation was conducted using the ratio of coefficients approach. Using metaanalysis, an additional eight published randomized clinical trials on the association of dairy consumption with systolic blood pressure were summarized.

Results Compared with the CC genotype (CC is associated with complete lactase deficiency), the CT/TT genotype (TT is associated with lactose persistence, and CT is associated with certain lactase deficiency) of LCT-13910 (lactase persistence gene) rs4988235 was associated with higher dairy consumption (0.23 (about 55 g/day), 95% confidence interval 0.17 to 0.29) serving/day; P<0.001) and was not associated with systolic blood pressure (0.31, 95% confidence interval −0.05 to 0.68 mm Hg; P=0.09) or risk of hypertension (odds ratio 1.01, 95% confidence interval 0.97 to 1.05; P=0.27). Using LCT-13910 rs4988235 as the instrumental variable, genetically determined dairy consumption was not associated with systolic blood pressure (β=1.35, 95% confidence interval −0.28 to 2.97 mm Hg for each serving/day) or risk of hypertension (odds ratio 1.04, 0.88 to 1.24). Moreover, meta-analysis of the published clinical trials showed that higher dairy intake has no significant effect on change in systolic blood pressure for interventions over one month to 12 months (intervention compared with control groups: β=−0.21, 95% confidence interval −0.98 to 0.57 mm Hg). In observational analysis, each serving/day increase in dairy consumption was associated with −0.11 (95% confidence interval −0.20 to −0.02 mm Hg; P=0.02) lower systolic blood pressure but not risk of hypertension (odds ratio 0.98, 0.97 to 1.00; P=0.11).

Conclusion The weak inverse association between dairy intake and systolic blood pressure in observational studies was not supported by a comprehensive instrumental variable analysis and systematic review of existing clinical trials.

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Association between clinically recorded alcohol consumption and initial presentation of 12 cardiovascular diseases: population based cohort study using linked health records

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Objectives To investigate the association between alcohol consumption and cardiovascular disease at higher resolution by examining the initial lifetime presentation of 12 cardiac, cerebrovascular, abdominal, or peripheral vascular diseases among five categories of consumption.

Design Population based cohort study of linked electronic health records covering primary care, hospital admissions, and mortality in 1997-2010 (median follow-up six years).

Setting CALIBER (ClinicAl research using LInked Bespoke studies and Electronic health Records).

Participants 1 937 360 adults (51% women), aged ≥30 who were free from cardiovascular disease at baseline.

Main outcom e measures 12 common symptomatic manifestations of cardiovascular disease, including chronic stable angina, unstable angina, acute myocardial infarction, unheralded coronary heart disease death, heart failure, sudden coronary death/cardiac arrest, transient ischaemic attack, ischaemic stroke, intracerebral and subarachnoid haemorrhage, peripheral arterial disease, and abdominal aortic aneurysm.

Results 114 859 individuals received an incident cardiovascular diagnosis during follow-up. Non-drinking was associated with an increased risk of unstable angina (hazard ratio 1.33, 95% confidence interval 1.21 to 1.45), myocardial infarction (1.32, 1.24 to1.41), unheralded coronary death (1.56, 1.38 to 1.76), heart failure (1.24, 1.11 to 1.38), ischaemic stroke (1.12, 1.01 to 1.24), peripheral arterial disease (1.22, 1.13 to 1.32), and abdominal aortic aneurysm (1.32, 1.17 to 1.49) compared with moderate drinking (consumption within contemporaneous UK weekly/daily guidelines of 21/3 and 14/2 units for men and women, respectively). Heavy drinking (exceeding guidelines) conferred an increased risk of presenting with unheralded coronary death (1.21, 1.08 to 1.35), heart failure (1.22, 1.08 to 1.37), cardiac arrest (1.50, 1.26 to 1.77), transient ischaemic attack (1.11, 1.02 to 1.37), ischaemic stroke (1.33, 1.09 to 1.63), intracerebral haemorrhage (1.37, 1.16 to 1.62), and peripheral arterial disease (1.35; 1.23 to 1.48), but a lower risk of myocardial infarction (0.88, 0.79 to 1.00) or stable angina (0.93, 0.86 to 1.00).

Conclusions Heterogeneous associations exist between level of alcohol consumption and the initial presentation of cardiovascular diseases. This has implications for counselling patients, public health communication, and clinical research, suggesting a more nuanced approach to the role of alcohol in prevention of cardiovascular disease is necessary.