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Can traditional risk factors explain the higher risk of cardiovascular disease in South Asians compared to Europeans in Norway and New Zealand?

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Topic: Social inequalities in cardiovascular health

Introduction: Immigrants from South Asia have increased risk of cardiovascular disease (CVD) compared to Europeans. The reasons for this excess risk are unclear, and the role of traditional risk factors is unsettled. The prospective relations between risk factors and subsequent CVD in South Asian populations have been scarcely studied.

Purpose The purpose of this study was to examine ethnic differences between South Asians and Europeans living in Norway and New Zealand in the risk of having a first CVD event, and to examine whether traditional risk factors (blood pressure, lipids, diabetes and smoking) could explain any such difference. Our purpose was also to describe the prospective relation between cardiovascular risk factors and subsequent first CVD events in South Asians and Europeans.

Methods: We used data from two different cohorts; a Norwegian (Cohort of Norway, n = 16 606) and a New Zealand cohort (PREDICT-CVD, n = 129 449) with information about ethnicity, cardiovascular risk factors and subsequent CVD through linkages with hospital registry data and causes of death registers in both countries. The two cohorts were analyzed separately. We used Cox proportional hazards regression to calculate hazard ratios (HRs) for CVD in South Asians versus Europeans and to study the prospective relation between risk factors and subsequent first CVD.

Results: South Asians in both Norway and New Zealand had higher total cholesterol /high density lipoprotein ratio and higher diabetes prevalence at baseline than Europeans, but lower levels of systolic blood pressure and smoked less (especially women). The cardiovascular risk factors were in general positively associated with CVD in both ethnic groups, across gender and country. South Asians of both genders in Norway and New Zealand had increased risk of CVD compared to the European majority populations being 87-92% higher in the Norwegian cohort and 42-75% higher in the New Zealand cohort. After having adjusted for blood pressure, lipids, diabetes and smoking, South Asians in both countries remained at having significantly increased risk of CVD with hazard ratios (HRs) for South Asians vs Europeans in the Norwegian cohort being 1.57; 95% CI 1.19-2.07 in men and 1.76; 95% CI 1.09-2.82 in women and HRs for South Asians vs Europeans in the New Zealand cohort being 1.64; 95% CI 1.43-1.88 in men and 1.39; 95% CI 1.11-1.73 in women.

Conclusion: Differences in distribution of cardiovascular risk factors seemed to explain some, but not all, of the excess risk of CVD in South Asians compared to Europeans in Norway and New Zealand.

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Social inequalities in the burden of stroke in Germany: cross-sectional analysis of a nationwide population-based health survey

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Topic: Social inequalities in cardiovascular health

Background: Social inequalities in stroke risk and outcomes have been reported for many countries. Knowledge of existing inequalities in specific countries and populations is important for effective stroke prevention and management.

Purpose: To examine (1) the association between socioeconomic status (SES) and the prevalence of stroke and (2) health inequalities among stroke survivors in the general population in Germany.

Methods: We analysed pooled data from waves 2009, 2010 and 2012 of the nationwide population-based study German Health Update (GEDA) with a total of 62,446 participants aged ≥ 18 years. Data on self-reported physician-diagnosed stroke, sociodemographic characteristics, chronic diseases, health status, and healthcare utilization were collected by standardized computer-assisted telephone interviews. Socioeconomic status (SES) was classified as low, medium and high using an index based on information on education, occupational status and net equivalent income. The association between SES and stroke prevalence was examined in multivariable logistic regression analysis. Differences between SES groups in health status and healthcare use after stroke were examined by regression models that included interaction terms for SES*stroke and that were adjusted for sociodemographics and comorbidities.

Results: The lifetime prevalence of stroke among adults in Germany was 2.5% overall, 2.4% in women and 2.6% in men. Prevalence ranged from 1.6% in people with high SES to 2.4% in those with medium and 4.1% in those with high SES (p(trend)<0.001). In age- and sex-stratified analyses, similar social gradients existed in all subgroups. Adjusting for age, sex, region, community size and study wave, a lower SES was associated with significantly higher odds of stroke (odds ratio (OR) for medium vs. high SES, 1.4 (95% CI, 1.2-1.6); OR for low vs. high SES, 1.9 (95% CI, 1.5-2.4)). Adjusting for all sociodemographics and comorbidities, participants with a lifetime history of stroke more often reported bad or very bad self-rated health (OR, 1.9; 95% CI, 1.6-2.3), severe global activity limitations in the last 6 months (OR, 1.8; 95% CI, 1.5-2.2), frequent mental distress in the last 4 weeks (OR, 1.4; 95% CI, 1.2-1.8), and at least one hospital admission in the last 12 months (OR 1.8; 95% CI, 1.5-2.1), compared to participants without stroke. No difference between SES groups were found for these health outcomes (all p for interaction SES*stroke > 0.1).

Conclusions: Lower SES is associated with higher stroke prevalence among adults in Germany. This social gradient is found in men and women and across all age groups and persists after adjustment for sociodemographic confounders. Lifetime history of stroke is associated with poorer health status and use of hospital admission independently of comorbidities in adjusted analyses, but outcomes did not differ between SES groups.

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Elevated resting heart rate in combination with vital exhaustion increases the risk of death from ischemic heart disease in the general population: the Copenhagen City Heart Study

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Topic: Psycho-social risk factors

Background: Vital exhaustion (VE) – a measure of fatigue, hopelessness and depression – has been shown as an independent risk factor for ischemic heart disease (IHD) in the general population. In addition, resting heart rate (RHR) has been observed as an independent predictor of cardiovascular mortality. It is possible that both factors act through the same underlying mechanisms, and thus they may potentiate each other in affecting risk of death from IHD. However, this remains so far unknown.

Purpose: To investigate the interplay between VE, RHR and IHD mortality in the general population.

Methods: Participants from the third wave of the Copenhagen City Heart Study (1991-1994) without history of IHD or atrial fibrillation were followed for fatal IHD (ICD-10: I20-I25) until the end of 2012. The final sample included 8810 participants (5009 females and 3801 males) aged 21 – 94 years (mean 57.1, s.d. 15.2). Data were collected at baseline through self-administered questionnaires and bio-clinical assessments. A questionnaire with 17 dichotomous items was used to assess level of VE. RHR was read from a 12-lead ECG at rest. Statistical analyses were performed using Analysis of Covariance, and Cox proportional regression modeling adjusted for conventional cardiovascular risk factors, educational level and income.

Results: During the median follow-up time of 19 years, 583 persons died from IHD. At baseline, the association between VE and RHR depended on sex (P for interaction term <0.05). In men, gradually higher RHR was observed with higher levels of VE, independent of age and socio-economic status. In women, no significant independent relation was shown. Both VE and RHR significantly and independently increased the risk for IHD mortality, also after stepwise adjusting for age, sex, cardiovascular risk factors and indicators of low socio-economic status (VE: fully adjusted HR per unit increase 1.04; 95%CI 1.03-1.06 and RHR: fully adjusted HR per 10 bpm increase 1.04; 95% CI 1.00-1.08). We further examined the combined exposure to low vs. high levels of VE (high level defined as minimum 5 on the 0-17 scale; prevalence 24.7%) and RHR (high level defined as minimum of 80 bpm; prevalence 27.3%) (Figure 1). Neither high VE nor high RHR alone were significantly associated with fatal IHD, but the combination of both high VE and high RHR significantly increased the risk for IHD mortality compared with the combination of low VE and low RHR (fully adjusted HR 1.87; 95% CI 1.40-2.50).

Conclusions: The combination of high RHR with VE synergistically increased the risk for death from IHD in a general population free from baseline cardiovascular disease. Both factors are easy to screen in primary care setting, hence these findings might have relevant implications for clinical practice.

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Figure 1. Multiple Cox regression results for fatal IHD by combined exposure to RHR and VE
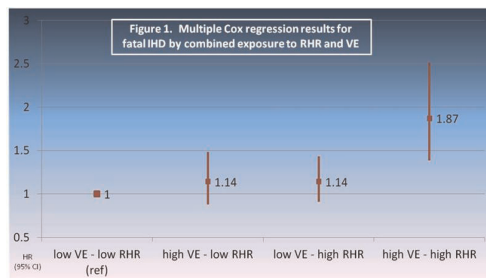
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Association between dietary fat intake and coronary heart disease in middle-aged and senior adults. The Hordaland Health Studies (HUSK).

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Topic: Epidemiology

Background: The association between type of dietary fat and the risk of coronary heart disease (CHD) remains debatable. Several risk factors for coronary heart disease (CHD) have been observed to be less pronounced among senior adults than among middle-aged adults given the importance of advancing age as a key risk factor for CHD, but age-differences in the importance of dietary intakes have not been evaluated.

Purpose: To investigate the association between different dietary fat intakes and incident CHD in middle-aged and senior adults.

Methods: We included in the analyses 5517 men and women aged 47–49 (N = 2995) and 71–74 (N = 2522) years participating in the Hordaland Health study (HUSK) without history of CHD who completed a 169-item food frequency questionnaire in 1997–99 (baseline). They were followed until 31 December 2009 for a coronary event (either hospitalization or death due to CHD). The associations between type of dietary fat and CHD were explored using Cox regression analysis. Results are provided as hazard ratio (HR) and 95% confidence intervals (CI). We modeled isocaloric substitution analysis to evaluate the effect of substituting part of the total energy intake from one dietary source with a different dietary source. Analyses were adjusted for age, gender, diabetes, hypertension, physical activity, smoking, body mass index and cholesterol intake.

Results: During a median follow-up of 10.9 years, we documented 112 incident cases in the middle-aged population and 492 incident cases among senior adults. In the middle-aged adults, a higher intake of monounsaturated fatty acids (MUFA) was significantly associated with reduced risk of CHD (HR for the highest versus the lowest quintile 0.46, 95% CI: 0.24–0.90). P trend for intake of MUFA in the middle-aged population was 0.01. Saturated fat (SFA) and polyunsaturated fat (PUFA) intake was not associated with the risk of CHD in either senior adults or middle-aged adults. An isocaloric substitution with 5% of energy intake from MUFA for 5% of energy intake from SFA (HR: 0.57, 95% CI: 0.34 − 0.95), PUFA (HR: 0.56, 95% CI: 0.34 − 0.94), protein (HR: 0.57, 95% CI: 0.34 − 0.95) or carbohydrates (excluding sugar) (HR: 0.50, 95% CI: 0.31 − 0.79) was associated with a lower CHD risk in the middle-aged population. No significant results were found among senior adults.

Conclusions − In this Norwegian population we observed that a higher intake of MUFA was associated with a decreased risk of CHD in the middle-aged population. Based on our modeled substitution analysis, it seems that substitution of different macronutrients with MUFA may be associated with a lower CHD risk in the middle-aged population.

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Epicardial adiposity, regardless of visceral adiposity, is associated with significant cardiovascular abnormalities in untreated and asymptomatic subjects, as measured by the calcium score

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Topic: Obesity

Background: It has been postulated that excess epicardial fat (ECF) is associated with cardiovascular disease (CVD) risk, yet a detailed association with calcium deposits has not been reported.

Methods: We screened 2490 asymptomatic subjects for CVD risk using ECVDRS, which consists of 10 tests: large (C1) and small (C2) artery stiffness, BP at rest and post mild exercise (PME), CIMT, abdominal aorta and left ventricle ultrasound, retinal photography, micro-albuminuria, ECG, and pro-BNP. 94 subjects underwent additional screening using CT scan to assess ECF in millimeters as well as calcium deposits.

Results: The mean calcium score (CS) was higher for subjects with epicardial fat, irrespective of their level of visceral adiposity. Non-obese subjects with excess ECF had an average CS of 265, whereas the non-obese with normal ECF had a mean CS of only 107. Similarly, the obese with excess ECF had a significantly higher mean CS than the obese without excess ECF. See Figure 1 for detailed results.

Conclusions: 1) Abnormal levels of both micro and macrovascular stiffness were significantly higher in subjects with excess ECF than in those with normal ECF, irrespective of visceral obesity, indicating that excess ECF is linked with vascular dysfunction. 2) The mean CS for non-obese subjects with excess ECF was more than two and a half times higher than that of the non-obese with normal ECF. This strongly suggests that excess ECF is associated with an elevated CS. 3) Notably, the CS was higher in the non-obese with excess ECF than in the obese with excess ECF, indicating that epicardial adiposity—and not visceral obesity—may play a larger role in CV structural and functional abnormalities than previously thought.

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Attainment of blood pressure, lipids and diabetes targets in people at high cardiovascular risk in Europe: a report from the EUROASPIRE IV Survey

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Topic: Epidemiology

Purpose: The EUROASPIRE IV (EA IV) survey in primary care was carried out by the European Society of Cardiology, EURObservational Research Programme in 2014-2015 and investigated risk factor management in patients at high cardiovascular (CVD) risk in14 European regions. The aim was to provide an audit of the Joint European Societies' guidelines on CVD prevention in people at high CVD risk in general practice and to see whether the practice of preventive cardiology had improved by comparison with the previous EUROASPIRE III (EA III) survey in 2006-2007.

Methods: All patients were free of coronary or other atherosclerotic disease but considered at high CVD risk since they had been started on blood pressure (BP) and/or lipid and/or glucose lowering treatments. They were interviewed and examined by means of standardized methods ≥6 months after the start of therapy.

Results: 4579 high CVD risk individuals (58% females), mean age 59 (SD 11) years, were interviewed and examined (participation rate 68%). The risk factor control was very poor, with less than half (43%) of the patients on BP lowering medication reaching the target of <140/90 mmHg (< 140/80 mmHg in people with self-reported diabetes). Among treated dyslipidaemic patients only 33% attained LDL-cholesterol (LDL-C) target of <2,5 mmol/L. Among treated type 2 diabetic patients, 59% achieved the HbA1c target of < 7.0mmol/L. However, many patients on no antihypertensive or lipid-lowering medications had elevated blood pressure (46%) and elevated LDL-cholesterol (89%). The use of BP lowering medication in people with hypertension was ACE inhibitors/ARBs 80%, calcium channel blockers 29%, diuretics 38%, beta-blockers 37%. Among people on lipid-lowering medication, statins were prescribed in 96% and fibrates in 6%. The comparison with EUROASPIRE III in the same centres participating in both surveys showed that the risk factor management remained poor. BP was below guideline recommended targets in 28% in EA III and 35% in EA IV; the LDL-C was < 2.5 mmol/L in 29% in EA III and 37% in EA IV and HbA1c was < 7% and 62% in EA III and 60% in EA IV.

Conclusions: The EA IV survey showed that large proportions of patients at high CVD risk have uncontrolled blood pressure, lipids and diabetes with most patients not achieving the targets defined in the prevention guidelines. There is still further potential to improve the management of patients at high CVD risk in Europe.

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Central vs. Cardiac Obesity

Epicardial Fat (ECF)	Non-obese subjectsBMI < 30[47 subjects]		Obese subjectsBMI >/= 30[47 subjects]	
	Normal ECFECF < 110 mm[24 subjects]	Excess ECFECF >/= 110[23 subjects]	Normal ECFECF < 110 mm[6 subjects]	Excess ECFECF >/= 110[41 subjects]
Mean Age	58	60	57	58
Mean BMI	26.1	25.8	31.5	34.9
Mean Rasmussen Risk Score (RRS)	4	7	6	7
Macro-arterial Stiffness (C1)	83% normal[20 out of 24] 17% abnormal[4 out of 24]	70% normal[16 out of 23] 30% abnormal[7 out of 23]	100% normal[6 out of 6] 0% abnormal[0 out of 6]	85% normal[35 out of 41] 15% abnormal[6 out of 41]
Micro-arterial Stiffness (C2)	88% normal[21 out of 24] 12% abnormal[3 out of 24]	65% normal[15 out of 23] 35% abnormals[8 out of 23]	83% normal[5 out of 6] 17% abnormal[1 out of 6]	63% normal[26 out of 41] 37% abnormal[15 out of 41]
Carotid Intima-Media Thickness (CIMT)	67% normal[16 out of 24] 33% abnormal[8 out of 24]	57% normal[13 out of 23] 43% abnormal[10 out of 23]	50% normal[3 out of 6] 50% abnormal[3 out of 6]	46% normal[19 out of 41] 54% abnormal[22 out of 41]
Mean Calcium Score (CS)	107	265	20	202

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Translation of evidence from 11 randomized clinical trials on statin use in primary prevention of cardiovascular disease into ESC 2016 and ACC/AHA 2013 guidelines: results from the Rotterdam Study

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Topic: Epidemiology

Background: Evidence from randomized clinical trials (RCTs) constitutes the base of the European Society of Cardiology (ESC) 2016 and American College of Cardiology/ American Heart Association (ACC/AHA) 2013 guidelines for lipid-lowering treatment in primary prevention of atherosclerotic cardiovascular disease (ASCVD).

Purpose: To quantify the contribution of 11 primary prevention RCTs to the practical application of prevailing ESC and ACC/AHA guidelines.

Methods: From 1997-2008, 7279 participants aged 45-75 y, free of ASCVD, from the prospective population-based Rotterdam Study cohorts were included (mean age 61.1 y; 58.2% women). Eligibility of each participant was verified for every 1 of 11 double-blind placebo-controlled RCTs on statin use in primary prevention of ASCVD, as well as for positive recommendations on initiation of lipid-lowering therapy based on ESC 2016 and ACC/ AHA 2013 guidelines. Based on a mean 7.1 y follow-up, we calculated incidence rates (IRs) per 1000 person-years (pys) for fatal and non-fatal ASCVD combined.

Results: The proportion of participants eligible for each of the 11 RCTs ranged from 0.4% for ALLHAT-LLT to 30.8% for MEGA. A clear relationship was observed between the likelihood of ESC and ACC/AHA guideline recommendations for lipid-lowering treatment and the observed ASCVD IR (Figure). Among trial eligible individuals, the proportion of individuals meeting positive guideline recommendations was lowest for low-to-intermediate risk trials, including HOPE-3 (IR 7.8 per 1000 pys; ESC 12.1%; ACC/AHA 66.0%), MEGA (IR 10.3 per 1000 pys; ESC 26.4%; ACC/AHA 55.5%), and JUPITER (10.6 per 1000 pys; ESC 27.1%; ACC/AHA 68.1%), whilst RCTs done in diabetics (MRC/BHF HPS, CARDS, and ASPEN; IRs >15.1 per 1000 pys; ESC >93.4%; ACC/AHA >92.4%), or older individuals (PROSPER; IR 23.6 per 1000 pys; ESC 90.0%; ACC/AHA 99.6%) had virtually complete alignment with recommendations from both guidelines. Eligibility for an increasing number of RCTs correlated with a greater likelihood of being recommended lipid-lowering treatment by either guideline (ESC P=0.031; ACC/AHA p<0.001). Nearly half (48.1%) of the individuals younger than 65 years who died from ASCVD during follow-up would not qualify for lipid-lowering treatment based on the 2016 ESC prevention guidelines.

Conclusions: Compared to RCTs done in high risk populations, RCTs targeting low-to-intermediate risk populations are less well-reflected in the ACC/AHA, and even less so in the ESC guideline recommendations for primary prevention of ASCVD. Importantly, the low-to-intermediate risk population targeted by HOPE-3, the most recent RCT in this field, is not well-captured by the current European prevention guidelines and should be specifically considered in future iterations of the guidelines.

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ESC and ACC/AHA recommendations per RCT
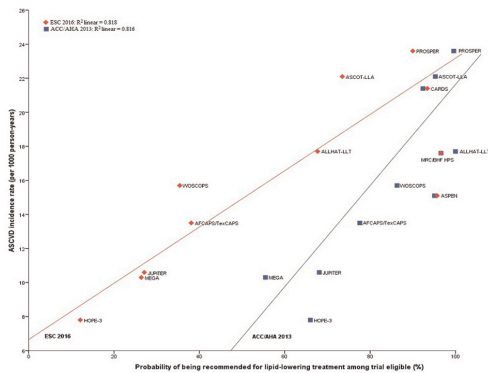
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The association between education level and cardiovascular disease incidence is partially mediated by uncontrolled diabetes and hypertension and by smoking

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Topic: Social inequalities in cardiovascular health

Background: An inverse association between education and cardiovascular (CV) disease incidence has been consistently observed. However, which are the mediating factors is not entirely clear.

Purpose: To determine the mediating role of classical CV risk factors, lifestyles and treatments in the association between education level and CV disease (CVD) incidence in a population-based cohort.

Methods: We used the REGICOR population cohorts recruited in 1995, 2000 and 2005 in north-eastern Spain. Participants underwent a physical examination and completed interview-administered questionnaires at baseline and follow-up. Participants were followed for CV events by interviews and data linkage. We included participants without previous CVD or missing data (n=9233). We first analysed the causal association between education and CVD incidence at 6 years of follow-up using marginal structural models with education-and-censoring inverse probability weights. Mediation of this association was assessed with structural equation modelling based on logistic regression and diagonally weighted least-squares estimation.

Results: Participants with a university degree had a CVD incidence hazard ratio of 0.51 (95% confidence interval (CI): 0.30-0.85) compared to those with primary or lower education. There was no effect modification be age or sex. Diabetes, hypertension and smoking were mediators of this association while body mass index, physical activity and dyslipidemia were not. Diabetes, hypertension, and smoking mediated 38% of the association between education and CVD incidence. The effect of diabetes and hypertension was due to uncontrolled glucose and blood pressure levels [indirect effect (95% CI)= a1*b1= -0.044 (-0.071, -0.017) and a3*b3= -0.018 (-0.030, -0.006), respectively]. The effect of smoking was a4*b4= 0.007 (0.001, 0.013). The significant pathways from education to mediators and from mediators to CVD incidence, with all the individual effects (a1-a4 and b1-b4), are depicted in the mediation figure.

Conclusions: The association between education level and CVD incidence at 6 years in the REGICOR cohorts was partly mediated by smoking and by uncontrolled diabetes and hypertension. These results suggest that improving smoking cessation rates and glucose and blood pressure control could diminish part of the education inequalities associated to a higher CVD risk.

Mediation figure