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### B-TYPE NATRIURETIC PEPTIDE PERFORMS BETTER THAN CURRENT CARDIOVASCULAR RISK SCORES IN IDENTIFYING SILENT "PANCARDIAC" TARGET ORGAN DAMAGE IN ALREADY TREATED PRIMARY PREVENTION PATIENTS

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**Background** Primary prevention needs to be improved because up to 70% of cardiovascular (CV) events occur outwith those classified as high risk by CV risk scores currently used in clinical practice (eg, Framingham). One possible way to improve primary prevention of CV disease is to identify those patients who may already harbour silent pancardiac target organ damage in the form of left ventricular hypertrophy (LVH), systolic dysfunction (LVSD), diastolic dysfunction (LVDD), left atrial enlargement (LAE) or silent myocardial ischaemia. This could be achieved by reapplying traditional CV risk scores to primary prevention patients after they have been treated or by screening with a simple biomarker like B-type natriuretic peptide (BNP).

**Methods** We prospectively recruited 300 asymptomatic individuals without known cardiovascular disease already on primary prevention therapy. Patients with valvular heart disease, atrial fibrillation and renal impairment were excluded. We measured BNP and calculated 10-year global CV risk scores (based on Framingham, QRISK and ASSIGN) in each participant. Transthoracic echocardiography was used to assess LV mass, LV systolic and diastolic function, and left atrial volume while the presence of inducible ischaemia was assessed by dobutamine stress echocardiography or dipyridamole myocardial perfusion imaging. Patients were divided into low, intermediate and high risk groups based on 10-year global CV risk. The prevalence of various cardiac TOD in each group was compared and ROC curves were constructed for BNP and for 10-year global CV risk scores to assess their ability to detect presence of silent cardiac TOD.

**Results** One hundred and two (34%) patients (Mean age 64±6.0 years, 58% males) had evidence of silent cardiac TOD (29.7% LVH, 18% LAE, 17.3% LVDD, 7.3% LVSD and 6.3% Ischaemia). The prevalence of cardiac TOD ranged from 19 to 28% in the low risk, 26%–33% in the intermediate risk and 36%–41% in the high risk groups based on three commonly used CV risk equations. BNP levels were significantly higher (median (IQR); 21.6 (13.6–40.0) vs 11.4 (6.3–20.0) pg/ml,  $p<0.0001$ ) in those with cardiac TOD compared to those without. The AUC for BNP to identify any form of cardiac TOD was 0.77 ( $p<0.0001$ ) overall and 0.83 ( $p<0.0001$ ) in males. However, discrimination power of CV risk scores was poor with area under curve of only 0.58 ( $p=0.02$ ) for QRISK, 0.62 ( $p=0.001$ ) for Framingham and 0.62 ( $p=0.001$ ) for ASSIGN to detect presence of any form of TOD.

**Conclusion** Silent cardiac TOD is highly prevalent (34%) in already treated primary prevention population but current CV risk estimation alone performs poorly in the detection of these silent cardiac abnormalities. However, a raised BNP is able to identify existing silent cardiac TOD of various subtypes particularly in males. Using BNP to identify silent cardiac TOD could, in the future, become a new way to improve the primary prevention of CV events.

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### CAN MICROALBUMINURIA IDENTIFY SILENT "PANCARDIAC" TARGET ORGAN DAMAGE IN A NON-DIABETIC PRIMARY PREVENTION POPULATION?

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**Background** Microalbuminuria is associated with increased cardiovascular mortality and is a marker of generalised vascular dysfunction.

We sought to investigate whether microalbuminuria identified the presence of silent "pancardiac" target organ damage (TOD) ie, left ventricular hypertrophy (LVH), systolic dysfunction (LVSD), diastolic dysfunction (LVDD), left atrial enlargement (LAE) or silent myocardial ischaemia in a non-diabetic primary prevention population.

**Methods** Two hundred and sixty-three asymptomatic individuals without diabetes or previous cardiovascular disease on primary preventive therapy were prospectively recruited. Each participant underwent a comprehensive echocardiographic examination for the assessment of LV mass, LV systolic and diastolic function, and left atrial volume while the presence of inducible ischaemia was assessed by dobutamine stress echocardiography or dipyridamole myocardial perfusion imaging. A spot urine sample was analysed for microalbuminuria and urinary creatinine by a trained laboratory technician blinded to clinical or echocardiographic data. Microalbuminuria was defined as urinary albumin to creatinine ratio of  $\geq 2.5$  mg/mmol in males and  $\geq 3.5$  mg/mmol in females.

**Results** Out of 263 participants (Mean age 64±6.3 years, 57% males) 89 (33.8%) had evidence of silent cardiac TOD (29.7% LVH, 16.7% LAE, 17.1% LVDD, 6.8% LVSD and 6.1% Ischaemia). The prevalence of cardiac TOD was significantly higher (53% vs 29%,  $p=0.002$ ) among those with microalbuminuria than those without. In multivariate analysis adjusted for age, gender, hypertension and dyslipidemia, presence of microalbuminuria was an independent predictor of cardiac TOD with an adjusted HR of 2.54 (95% CI, 1.2 to 4.4,  $p=0.005$ ). The utility of UACR in discriminating between those with or without cardiac TOD was assessed by receiver operating characteristic analysis but the area under curve was only  $0.61\pm 0.04$ ,  $p=0.003$ .

**Conclusion** Microalbuminuria is an independent predictor of silent "pancardiac" target organ damage in a non-diabetic primary prevention population. Presence of microalbuminuria may help to identify those primary prevention patients who are at a particularly higher risk.

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### GENE-GENE INTERACTIONS IN CORONARY ARTERY DISEASE

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**Background** Only a small fraction of the heritability of coronary artery disease (CAD) has been explained by common variants identified by genome-wide association studies. Among the stones to be turned in the hunt for the missing heritability of CAD are gene-gene interactions. We investigated whether interactions between common alleles in genes and pathways of known importance to cardiovascular regulation may contribute to the heritability of CAD.

**Methods** 2101 CAD cases and 2426 controls of Caucasian origin recruited into Wellcome Trust Case Control Consortium were genotyped using 50 K IBC gene-centric array containing 45 707 single nucleotide polymorphisms (SNPs) of the highest biological relevance to cardiovascular system. After applying appropriate quality control filters, 11 332 common (minor allele frequency >10%), independent ( $r^2$  linkage disequilibrium coefficient of  $\leq 0.5$ ) were included in pair-wise SNP-SNP interaction analysis using two complementary statistical approaches: logistic regression (PLINK and INTERSNP software packages) and Bayesian model (BEAM software).

**Results** None of the analysed SNP-SNP interactions was statistically significant after correction for multiple testing ( $p=7.8\times 10^{-10}$ ). The most significant interaction identified in this analysis was

between rs727139 (KCNH8) on chromosome 3 and rs11167496 (PDGFRB) on chromosome 5 ( $p=2.45 \times 10^{-8}$ ). Analysis of subsets of SNPs pre-selected based on their nominal association with CAD ( $p < 0.05$ ) or molecular functionality (non-synonymous SNPs) did not contribute more significant findings than investigation of random set of SNPs.

**Conclusion** Our analysis suggests that common SNP-SNP interactions are unlikely to account for a large proportion of the missing heritability of CAD.

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#### CLINICAL AND FINANCIAL REPERCUSSIONS OF THE MARCH 2010 NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE (NICE) GUIDELINE "CHEST PAIN OF RECENT ONSET" ON THE RAPID ACCESS CHEST PAIN CLINIC (RACPC)

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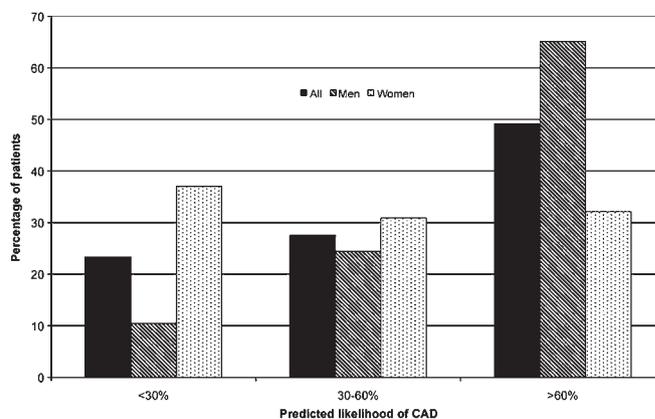
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**Background** The RACPC is a well-established "one-stop" service, with goal to identify patients with stable chest pain due to coronary artery disease (CAD) and quickly reassure those with non-cardiac pain. In March 2010, NICE published a new guideline, which advocates assessing likelihood of CAD based on age, gender, history and risk factors (RF). If estimated likelihood is  $>60\%$ , invasive coronary angiography (ICA) is recommended as the first-line diagnostic investigation. If estimated likelihood is  $30\%–60\%$ , functional imaging is recommended. If estimated likelihood is  $<30\%$ , CT calcium scoring CT coronary angiography (CTCA) is recommended. Significantly, the guideline discourages the use of ETT to diagnose or exclude stable angina in patients without known CAD.

**Methods** 167 consecutive patients referred to RACPC between October 2009 and March 2010 were retrospectively assessed for likelihood of CAD according to the new NICE guideline. Choice of investigations and eventual outcome (confirmed CAD vs no evidence of CAD) were compared between subgroups defined by estimated likelihood of CAD. An economic analysis of cost of investigation per patient was undertaken using current Payment by Results national tariffs.

**Results** Our patient population had a high prevalence of RF with 38.1% having a total of three or more RF. Consequently 23.2% of patients had an estimated likelihood of CAD of  $<30\%$ . 27.4% had an estimated likelihood of  $30\%–60\%$ . 49.4% had an estimated likelihood of  $>60\%$ . 7.2% of patients were lost to follow-up. 14.4% of patients were ultimately confirmed to have CAD on ICA, which correlated with pre-test estimated likelihood. 6% of patients with likelihood  $<30\%$ , 8.7% of those with likelihood  $30\%–60\%$  and 23.2% of those with likelihood  $>60\%$  were confirmed to have CAD. Average cost of investigation per patient was £528. A negative ETT resulted in average cost per patient of £347. An inconclusive ETT resulted in higher cost (£728) as did inability to exercise (£435) due to the need for further investigations. A positive ETT resulted in average cost of £1174 due to the high cost of ICA. Were the NICE guideline strictly applied to our patient population, average cost per patient would have been substantially higher at £838 (£362 per patient if likelihood  $<30\%$ , £566 if likelihood  $30\%–60\%$  and £1218 if likelihood  $>60\%$ ). Overall this corresponds to a 60% increase in cost.

**Conclusion** The 2010 NICE guideline appears to significantly overestimate the true risk in our patient population. Were the guideline strictly applied, almost half of our patients would proceed to ICA as a first-line investigation, but many of them would be found to have unobstructed coronary arteries. As ICA is an expensive investigation, this would inevitably result in a significant increase in average cost per patient. Relatively few patients would be eligible for CTCA, which is an excellent non-invasive "rule-out" test for CAD and relatively inexpensive compared with other investigations.



Abstract 56 Figure 1

Abstract 56 Table 1

	All	Men	Women
Numbers (%)	167	86 (51.5)	51 (48.5)
Age (mean $\pm$ SD)	56.0 $\pm$ 12.6	55.2 $\pm$ 13.3	57.0 $\pm$ 11.8
Diabetes (%)	29 (17.4)	15 (17.4)	14 (17.3)
Hypertension (%)	72 (43.1)	40 (46.5)	32 (39.5)
Hypercholesterolaemia (%)	100 (59.9)	53 (61.6)	47 (58.0)
Family history (%)	58 (34.7)	28 (32.6)	30 (37.0)
Smoking (%)	87 (52.1)	54 (62.8)	33 (40.7)
Systolic BP (mean $\pm$ SD) / Diastolic BP (mean $\pm$ SD)	134 $\pm$ 21 / 79 $\pm$ 11	131 $\pm$ 18 / 80 $\pm$ 11	137 $\pm$ 23 / 78 $\pm$ 10
Fasting glucose (mean $\pm$ SD)	5.2 $\pm$ 1.0	5.7 $\pm$ 1.0	5.3 $\pm$ 1.1
Total cholesterol (mean $\pm$ SD)	5.17 $\pm$ 1.04	5.06 $\pm$ 1.06	5.29 $\pm$ 1.01
LDL (mean $\pm$ SD) / HDL (mean $\pm$ SD)	3.19 $\pm$ 0.90 / 1.30 $\pm$ 0.43	3.14 $\pm$ 0.90 / 1.23 $\pm$ 0.46	3.33 $\pm$ 0.86 / 1.38 $\pm$ 0.38
BMI (mean $\pm$ SD)	30.1 $\pm$ 6.0	29.4 $\pm$ 4.9	30.9 $\pm$ 6.9

Abstract 56 Table 2

	Average cost per patient prior to NICE guideline implementation	Average cost per patient were NICE guideline strictly implemented
Predicted likelihood $<30\%$	£324	£362
Predicted likelihood $30\%–60\%$	£467	£566
Predicted likelihood $>60\%$	£661	£1218
OVERALL AVERAGE COST PER PATIENT	£528	£838

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#### THE IMPACT OF PREOPERATIVE RENAL DYSFUNCTION AND THERAPY TYPE IN PATIENTS WITH TYPE 2 DIABETES UNDERGOING CORONARY ARTERY BYPASS SURGERY

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**Introduction** There is limited data addressing the impact of preoperative renal dysfunction in type 2 diabetics (T2DM) undergoing first-time coronary artery bypass surgery (CABG); specifically exploring the influence of diabetic management (oral hypoglycaemic (OH) and insulin therapy (IN)). We assessed the impact of preoperative renal status and diabetic management on the post operative renal status, morbidity, 30-day and long-term survival in T2DM-CABG.

**Methods** We reviewed prospectively accrued data from 1/1/1999 to 31/12/2009. Pre and 4 to 5-day postoperative creatinine clearance