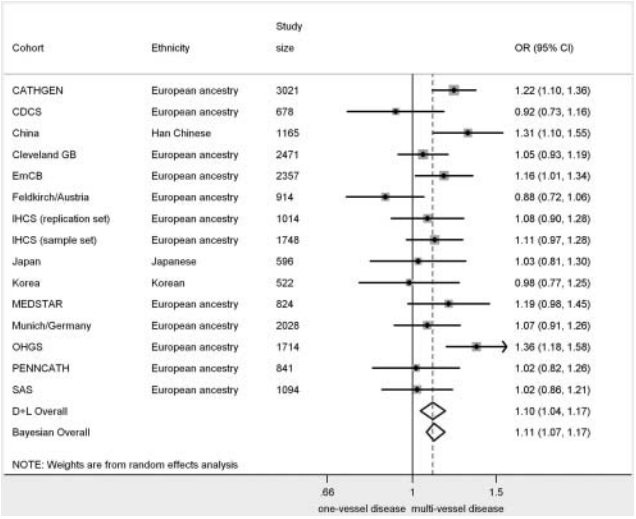

Figure 1 Association between 9p21 and multi-vessel disease as compared with single-vessel disease (Analysed with allelic Model, D+L Overall=Random effect analysis, Bayesian Overall=Bayesian analysis).

126

CHROMOSOME 9P21 LOCUS AND ANGIOGRAPHIC CORONARY ARTERY DISEASE BURDEN: A COLLABORATIVE META-ANALYSIS

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doi:10.1136/heartjnl-2013-304019.126

Background Chromosome 9p21 variants have been strongly associated with coronary heart disease in genome-wide association studies, but questions remain on the mechanism of risk, specifically whether the locus contributes to coronary atheroma burden or plaque instability. We investigated the relationship of 9p21 locus with (1) angiographic coronary artery disease (CAD) burden and (2) myocardial infarction (MI) in individuals with underlying CAD. Methods:We established a collaboration of 21 studies consisting of 33,673 subjects with information on both CAD (clinical or angiographic) and MI status along with 9p21 genotype. Tabular data were provided for each cohort on the presence and burden of angiographic CAD; MI cases with underlying CAD; and the diabetic status of all subjects.

Results We first confirmed an association between 9p21 and CAD using angiographically defined cases and controls (pooled OR=1.31 (95% CI 1.20 to 1.43)). Among subjects with angiographic CAD (n=20,987), random-effects model identified an association with multi-vessel CAD, compared to those with single-vessel disease (OR=1.10 (95% CI 1.04 to 1.17) per copy of risk allele). Genotypic models showed an OR of 1.15 (95% CI 1.04 to 1.26) for heterozygous carrier and 1.23 (95% CI 1.08 to 1.39) for homozygous carrier. Finally, there was no significant association between 9p21 and prevalent MI when both cases (n=17 791) and controls (n=15 882) had underlying CAD (OR=0.99 (95% CI 0.95 to 1.03) per risk allele).

Conclusions The 9p21 locus shows convincing association with greater burden of CAD, but not with MI in the presence of underlying CAD. This adds further weight to the hypothesis that 9p21 locus primarily mediates an atherosclerotic phenotype.