Appendix 4 Search strategy [posted as supplied by author]

Any studies with information on any polymorphisms or haplotypes in or near the *CRP* locus were eligible for inclusion in the CCGC. Both retrospective case-control and prospective study designs were eligible as they were used for the analysis of *CRP* gene variants and CHD. Studies were identified through computer-assisted literature searches of publication databases, scanning of reference lists, hand-searching of relevant journals and by direct contact with authors and principal investigators of studies with relevant designs, identified primarily through a registry of large, well-validated genetic studies of CHD. Electronic searches were performed using MEDLINE, EMBASE, Science Citation Index and Google Scholar databases. Combinations of the following keywords were entered into search engines using Subject Headings (eg, MeSH, Emtree) where possible: C-reactive Protein, CRP, gene(s), genet*, genot*, single nucleotide polymorphism(s), SNP(s), variants, cardiovascular disease, CVD, coronary disease, myocardial infarction, myocardial ischaemia, myocardial ischemia, MI, CHD, and atherosclerosis. Titles and abstracts were scanned for relevant review articles (including previous meta-analyses of CRP - CHD associations) and for studies with the relevant endpoints. Reference lists were scanned and relevant journals (eg, *JAMA, NEJM, Circulation, BMJ*, *Lancet, Atherosclerosis,* etc) were hand-searched for further studies. Figure A in appendix 3 summarises the search strategy used to identify 51 potential studies, of which 47 agreed to participate.

To increase the power and reliability of the analyses, relevant large studies in the Emerging Risk Factors Collaboration with data on circulating CRP and CHD outcomes and stored blood samples, were identified and investigators invited to join the CCGC. The availability of funding for this collaboration[1] enabled these studies to measure the four principal SNPs, thereby contributing new, unpublished data to the consortium. Searches were updated periodically and investigators of any additional studies found were also invited to join the collaboration. As almost all identified studies shared data (many of which have not reported their findings), this collaboration maximizes comprehensiveness and minimizes publication biases. Similarly because of the inclusion of all available data on gene, disease and intermediate phenotypes from each study, this collaboration should substantially reduce any biases associated with the selective publication of only significant or interesting associations.[2-4] By July 2010, all 47 included studies had contributed data on 194,418 participants, including 46,557 incident and prevalent CHD cases. About one third of the cases (ie, 10,981 incident and 5241 prevalent cases) and two thirds of participants (124,931) derived from 27 prospective studies, including 2 case-cohort studies,[5;6] 10 case-control studies "nested" in larger cohorts (5 frequency matched[7-10] and 5 individually matched[11-14]) and 15 cohort studies[7;15-26] contributing 540 thousand person-years at risk. The remaining

30,335 prevalent cases derived from 20 retrospective case-control studies (comprising 69,487 participants).[7;15;20;27-39]

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