

8.2.1.085 Associations of Known Blood Pressure-Related Genotypes with Cardiovascular and Renal Outcomes in a Prospective Setting
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Background: Recent meta-analyses of genome-wide studies (GWAS) have identified several common genetic variants related to blood pressure (BP) and hypertension. Each of these variants explains only a very small fraction of the variance of BP, but a genotype score constructed from several variants may explain a larger fraction. Furthermore, even small lifelong differences in BP levels may have a substantial influence on the risk of cardiovascular and renal complications of hypertension. It is well-known that elevated BP is a strong risk factor for stroke, myocardial infarction, heart failure, and renal failure. Altogether 14 single nucleotide polymorphisms (SNP), most of them unpublished at the moment but known to be associated with BP, have been genotyped in FINRISK 1992, 1997, 2002 and in Health 2000 participants (the adult sample of 30 + years old, n=6200), altogether about 32 000 individuals. These cohorts have been followed up at the moment until the end of 2008 for cardiovascular and renal events by record linkage with the national health care registers.

Aims: The aims of the present study are:

1. To examine cross-sectional associations of these 14 SNPs and the genotype score calculated from them with systolic and diastolic BP and hypertension. (It is likely that this will be published from the large meta-analyses before our study becomes ready).
2. To examine, in a prospective setting, the associations of these 14 SNPs and the genotype score calculated from them with the risk of incident stroke, myocardial infarction, heart failure and chronic kidney disease.
3. To examine, whether the genotype score of BP has interactions with "environmental" factors such as age, sex, BMI and alcohol consumption.

In addition to the three main aims mentioned above, we will analyze the associations of these 14 SNPs and the genotype score calculated from them with the risk of incident hypertension using drug reimbursement records as a proxy for incident hypertension. Furthermore, since we have just finished similar analyses on the genetic score of CHD in these same cohorts, we will in the present project analyze the joint effects of the BP score and CHD score.

Methodological aspects: The genotype score of BP will be calculated as the sum of risk alleles, weighting each allele by its effect in the original discovery sample. Using heart failure as an outcome requires validation of the heart failure diagnoses in the hospital discharge register, causes-of-death register and in the drug reimbursement register. A project examining

the validity of heart failure diagnoses has been recently initiated. If needed, we will review the heart failure diagnoses in these registers.

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Timeline: Data-analyses during the spring 2010, writing of the report during the summer and early autumn, submission for publication: late autumn 2010.

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