Definition of cardiopulmonary disease

Cardiopulmonary disease was defined to be present if the participant declared having preexisting disease or to have used health services for breathing problems in the 12 months prior to follow-up examination.
Pre-existing disease was considered present if the participant answered positively to any of the questions:
-'Do you have heart disease?'
-'Do you have emphysema?'
-'Do you have chronic bronchitis?'
Answer categories 'Yes, but not diagnosed by a doctor' and 'Yes, diagnosed by a doctor' were considered positive.

Health service use for breathing problems was considered present if a positive answer to one of the following questions was given:
-'Have you visited a hospital emergency room because of breathing problems in the last 12 months?'
-'Have you spent a night in hospital because of breathing problems in the last 12 months?'
-'Have you been seen by a general practitioner because of breathing problems or because of shortness of breath in the last 12 months?'
'Have you seen a specialist (chest physician, allergy specialist, internal medicine specialist, ENT doctor) because of your breathing problems or shortness of breath in the last 12 months?'

Genotyping procedures

Extraction of genomic DNA from EDTA-anticoagulated whole blood was performed manually using the PuregeneTM DNA Isolation Kit (Gentra Systems, Plymouth, MN, USA).

Genotyping of SNP rs6742078

Data on SNP rs6742078 was available from genome-wide genotyping done on the Illumina Human 610quad BeadChip in the framework of the EU-funded GABRIEL study [1], which is a large asthma consortium aiming to uncover its genetic and environmental determinants. 567'589 autosomal SNPs were successfully genotyped. Strict quality control (QC) was applied by excluding samples with <97% genotyping success rate, non-European origin, cryptic relatedness or sex-inconsistencies, as well as SNPs with Hardy-Weinberg equilibrium p-value$<10^{-4}$, call rate <97% and minor allele frequency (MAF) <5%. SNPs were imputed to

2.5 Mio using MACH v 1.0 software [2] and the HapMap v22 CEPH reference panel of Utah residents with ancestry from northern and western Europe.[3] SNP rs6742078 was originally genotyped, but in the current work, imputed data was used for analysis, as the imputation procedure fills missing genotyping information and the imputation quality was excellent (Rsq 1.0). Data for 982 non-asthmatic participants was available for the current study. Being free of asthma was defined as neither self-report nor doctors diagnosis of asthma using a standardized questionnaire.[4]

References:

1. Moffatt, M.F., et al., *A large-scale, consortium-based genomewide association study of asthma.* N Engl J Med, 2010. **363**(13): p. 1211-21.
2. Li, Y., et al., *MaCH: using sequence and genotype data to estimate haplotypes and unobserved genotypes.* Genet Epidemiol, 2010. **34**(8): p. 816-34.
3. International HapMap, C., *A haplotype map of the human genome.* Nature, 2005. **437**(7063): p. 1299-320.
4. Ackermann-Liebrich, U., et al., *Follow-up of the Swiss Cohort Study on Air Pollution and Lung Diseases in Adults (SAPALDIA 2) 1991-2003: methods and characterization of participants.* Soz Praventivmed, 2005. **50**(4): p. 245-63.