A polygenic architecture of medication-use across medical conditions

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Introduction: Genomics has been forecasted to revolutionise human health by improving medical treatment through a better understanding of the genetic epidemiology of human diseases. Despite great successes of the last decade's genome-wide association studies (GWAS), the results have to a limited extent been translated to genomic medicine. We propose, that one route to get closer to improved medical treatment is by understanding the genetics of medication-use. We hypothesise that, irrespectively of medical condition, medication-use *per se* has a unique genetic heritable architecture.

Methods: Medication-use from 335.744 individuals from the UK Biobank was obtained, and we conducted a GWAS on 9 million imputed genetic variants. We estimated the heritability of medication-use and partitioned the genetic variance across different categories. Using five-fold cross validation we performed within sample prediction of medication-use.

Results: We identified 57 independent loci associated with variation in medication-use and estimated that 14% of the total variation was attributable to common genetic variants. The largest fraction of genetic variance was captured by variants with low to medium minor allele frequency. In particular coding and conserved regions, as well as transcription start sites, displayed significantly enrichment of heritability. The mean prediction accuracy was 0.14.

Conclusion: These results demonstrate that medication-use *per se* is a complex trait irrespectively of medical condition. Thus, if the goal is to improve medical treatment it might be insufficient to solely rely on analyses of complex diseases as medication-use *per se* has its own genetic architecture.

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