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Consumption of medications with variable genetically-related effects in Dutch population

M. A. Alshabeeb[1], V. H. Deneer[2], F. W. Asselbergs[3,4]. [1]Medical Genomics Research Department, King Abdullah International Medical Research Center (KAIMRC), Riyadh, Saudi Arabia, [2]Department of Pharmacy, University Medical Center Utrecht, Utrecht University, Utrecht, Netherlands, [3]Department of Cardiology, Division of Heart and Lungs, University Medical Center Utrecht, Utrecht University, Utrecht, Netherlands, [4]Durrer Center for Cardiovascular Research, Netherlands Heart Institute, Utrecht, Netherlands.

Introduction: The clinical guidelines established by Dutch Pharmacogenetics Working Group (DPWG) stated significant genetic interactions that affect drug response of over 50 products (pharmacogenetics (PGX) drugs) (1). Specific genotyping tests can now be suggested for the reported drugs to protect highly susceptible individuals from serious adverse drug toxicities, to identify low or non-responders, to monitor drug-drug interactions and choose appropriate doses. This study aimed to determine the percentage of Dutch population who uses the drugs listed by DPWG, to identify the main prescribed PGX drug category and the major genes involved in drug interactions.

Method: The figures of drug consumption which involve insured population (more than 11 million) in all health centers in Netherlands are reported in GIP databank https://www.gipdatabank.nl/databank.asp. We analysed the consumption data of 45 PGX drugs over the period 2011-2015 and estimated their interactions with 15 genes. Frequency of risk alleles among Dutch population was obtained from the public database: Genome of the Netherlands (GONL) http://www.nlgenome.nl/.

Results: Over five year period, 34.7 million incidents (exposure of patients to PGX drugs) were reported with an average of 3 incidents per each drug user, Table 1. One quarter of the incidents (8.3 million, approximately) are considered risky since the exposed patients are possibly carrying the genetic mutations associated with reduced drug efficacy or contributed to adverse drug reactions' development. Up to 60% of the risky incidents (5 million) were related to administration of drugs metabolised by *CYP2D6*. *SLCO1B1* and *CYP2C19* were identified among the top genes affecting response to the used drugs (about 23% versus 12% of the risky incidents, respectively). Gastroenterology medications were the top PGX drug class prescribed (26%), followed by endocrinology and analgesic/anaesthesiology products (22% and 20%, respectively). Incidents related to cardiology and psychiatry/neurology medications were rated as fourth and fifth classes (14% and 12%, respectively).

Conclusion: Exposure of patients to PGX drug is a common practice in the Netherlands with an average of three incidents occur per patient over five-year period. This finding is similar to the results of an American study where half of the participants had one incident experience while one quarter to one third of them had two or more PGX exposures over four year time (2). *CYP2D6*, *SLCO1B1 and CYP2C19* were the most contributing genes involved in PGX drug interactions.

References:

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