Nature Reviews Cardiology | Published online 13 Oct 2016; doi:10.1038/nrcardio.2016.172

CORONARY ARTERY DISEASE

New polygenic risk score improves prediction of CHD

A risk score comprising >49,000 single-nucleotide polymorphisms (SNPs) improves prediction of the risk of coronary heart disease (CHD) relative to traditional clinical risk scores, according to an international study involving Professors Nilesh J. Samani, Veikko Salomaa, Samuli Ripatti, and Michael Inouye. "More than half of CHD events occur in persons who are not recognized by established non-genetic scores as having a high risk," remarks Salomaa.

The investigators demonstrated that the genomic risk score (GRS), generated with data from CARDIoGRAMplusC4D, was associated with incident CHD in five independent, prospective cohorts (three from the FINRISK study and two from the Framingham Heart Study) independently of known risk factors and established clinical risk scores. Furthermore, combining the GRS with the Framingham or ACC/AHA13 clinical scores improved the 10-year risk prediction, particularly for individuals aged ≥60 years. The GRS also captured lifetime risk trajectories, with men in the highest quintile of absolute risk reaching a clinically relevant 10% risk of CHD 12–18 years earlier than those in the lowest quintile. "If robust, this level of stratification could be quite valuable for disease prevention in the decades preceding a CHD event," points out Inouye.

"Our approach was to capture as much of the genome-wide variation as possible," says Ripatti. "This provides a much more precise description of an individual's genome-wide risk compared with earlier approaches," which either focused on individual, rare, high-impact gene variants or included only the lead SNPs from genome-wide association studies. Samani explains that future steps should include validation of the GRS in other ethnic groups, and assessment of the cost-effectiveness of genetic testing.

Irene Fernández-Ruiz

ORIGINAL ARTICLE Abraham, G. *et al.* Genomic prediction of coronary heart disease. *Eur. Heart J.* http://dx.doi.org/10.1093/eurheartj/ehw450 (2016)

FURTHER READING Wong, N. D. Epidemiological studies of CHD and the evolution of preventive cardiology. *Nat. Rev. Cardiol.* **11**, 276–289 (2014)