# Use of multiple genetic markers not linked with better risk prediction of CVD

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Creation of a genetic risk score comprised of multiple genetic markers associated with cardiovascular disease (CVD) was not associated with significant improvement in CVD risk prediction in a study that included more than 19,000 women, according to a study in the February 17 issue of *JAMA*.

"Risk prediction is a central part of cardiovascular disease prevention and refining prediction strategies remains important for targeting treatment recommendations. One area of potential improvement has been the discovery of genetic markers for cardiovascular disease as well as intermediate phenotypes [physical manifestations] such as cholesterol and blood pressure. Recent efforts using genome-wide association studies have greatly expanded the discovery of genetic markers associated with cardiovascular disease," the authors write. "While multiple genetic markers associated with cardiovascular disease have been identified by genome-wide association studies, their aggregate effect on risk beyond traditional factors is uncertain, particularly among women."

Nina P. Paynter, Ph.D., of Brigham and Women's Hospital, Boston, and colleagues, constructed two genetic risk scores based on a comprehensive literature-based selection of genetic markers known to be associated with either cardiovascular disease or an intermediate phenotype and tested the scores to assess their predictive ability. The study included 19,313 initially healthy white women in the Women's Genome Health Study, followed up over a median (midpoint) of 12.3

years. Genetic risk scores were constructed from the National Human Genome Research Institute's catalog of genome-wide association study results published between 2005 and June 2009.

A total of 101 single nucleotide polymorphisms (SNPs) reported to be associated with cardiovascular disease or at least 1 intermediate cardiovascular disease phenotype were identified and risk alleles (an alternative form of a gene) were added to create a genetic risk score. During follow-up, 777 cardiovascular disease events occurred (199 heart attacks, 203 strokes, 63 cardiovascular deaths, 312 coronary artery revascularizations).

After analysis, the researchers found an absolute cardiovascular disease risk of 3 percent over 10 years in the lowest tertile (group) of genetic risk (73-99 risk alleles) and 3.7 percent in the highest tertile (106-125 risk alleles). However, after adjustment for traditional factors, the genetic risk score was not associated with cardiovascular disease risk. "In contrast, family history of premature [heart attack] remained an independent risk factor for incident cardiovascular disease even after adjustment," the authors write.

"We believe these data have clinical relevance for several reasons. First, genome-wide testing is increasingly available and marketed to the general public. Our study finds no clinical utility in a multilocus panel of SNPs for cardiovascular risk based on the best available literature. Second, our data confirm the utility of intermediate phenotypes such as total cholesterol, high-density lipoprotein cholesterol, and blood pressure in as much as genetic risk scores were no longer significant after adjustment for these phenotypes," the researchers write. "Third, our findings confirm the importance of family history of cardiovascular disease, which integrates shared genetics, shared behaviors, and environmental factors. At the same time, we believe that our data suggest areas for further biomarker research, which may improve

prediction."

"While the importance of genetic data in understanding biology and etiology is unchallenged, we did not find evidence in this study of more than 19,000 women to incorporate the current body of known genetic markers into formal clinical tools for cardiovascular risk assessment."

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