Significant and rapid progress in genetics research and data analytics is currently enabling an unprecedented expansion in science’s understanding of the genetic underpinnings of rare and common diseases. Large-scale cohort studies such as the UK Biobank are helping scientists build powerful prognostic models for a number of diseases, including breast cancer and coronary artery disease, and hastening the development of a new tool for quantifying the inheritability of common diseases: Polygenic risk scores. RGA’s Richard Russell explains.

Genetic testing has commonly been used to search for high-penetrance single gene mutations known to cause the rarer Mendelian or monogenic diseases. However, most cases of major diseases such as coronary artery disease, diabetes and cancers are multifactorial in nature. This means the risk of actually developing one of these diseases is due to a combination of genetic and environmental factors, and the genetic mechanism is difficult to measure.

Since 2005, genome-wide association studies (GWAS) have enabled the discovery of differences in the DNA sequences of individuals with a disease compared to individuals without the disease. These genetic differences, known as single nucleotide polymorphisms (SNPs), are positions in the genome at which some individuals in the population have one particular nucleotide that differs from the one normally found in that place. In recent years, geneticists have combined the genetic risk information from the millions of SNPs discovered in GWAS in order to predict an individual’s predisposition to specific diseases or complex traits. The resultant genetic risk metric is called a polygenic risk score (PRS).

This article reviews recent developments in polygenic risk profiling and the predictive utility of PRSs in relation to a person’s susceptibility to two diseases: Breast cancer and coronary artery disease. We discuss the possibility of adverse selection where genetic information on disease risk is available for insurance purchasers but not underwriters. Additional research is imperative to understand how PRSs, and other advances in genomic medicine, could cause adverse selection if consumers use this information to alter their insurance purchasing behaviour.

Polygenic risk scores:
Quantifying the inheritability of common diseases

Genetic susceptibility
How informative are genetic test results for predicting major morbidities and mortality? Many researchers are now using large-scale cohorts such as UK to explore genetic information alongside traditional health risk factors. UK Biobank offers tremendous opportunities to research mortality and morbidity outcomes using both genetic and environmental risk factors.

Recent studies utilising UK Biobank data have begun to demonstrate the considerable potential for
PRSs to identify individuals at higher (and lower) risk of disease. Indeed, researchers have now developed PRSs for many common diseases and have shown their vast potential in risk prediction. For example, recent research about coronary artery disease risk and PRSs demonstrated that people with a PRS in the highest 5% in the UK Biobank data have a threefold increased risk of experiencing the condition compared to the remaining 95%.