Genomics plc welcomes Professor Sir Mike Richards' Independent Review of Adult Screening Programmes in England

Report highlights the potential of polygenic risk scores in cancer screening programmes using data from Genomics plc

Use of polygenic risk scores could identify higher risk patients requiring screening from an earlier age

Government's Accelerated Diagnosis of Disease programme will evaluate use of polygenic risk scores, developed by Genomics plc, to identify people at high risk of serious illness

16 October 2019, OXFORD, UK – Genomics plc welcomes and applauds the publication of Professor Sir Mike Richards' Independent Review of Adult Screening Programmes in England, released today. The company believes that the UK has a major opportunity to transform the health and care system to a "prevention first" model by using new genomic technology.

Amongst its key findings the report notes the potential for the use of polygenic risk scores to ascertain whether an individual is at high or low risk of a wide range of conditions, including cancers and heart disease. The review includes polygenic risk scores produced by Genomics plc for breast cancer which demonstrate that this genetic approach can identify women in their early 40's who have the same breast cancer risk as a typical woman in her early 50's and a low risk woman in her 60's. Use of polygenic risk scores would allow targeting of screening to high risk women at younger ages. It can also improve the interpretation of screening results and reduce the numbers of false positives.

To date, very few individuals have had their genomes assessed to allow the calculation of polygenic risk scores for common diseases. The review notes that this is set to change as the genomic revolution means that genomic assessments to create such polygenic risk scores is becoming both feasible and more affordable.

The review highlights the government's recent commitment of £79m to an Accelerated Diagnosis of Disease (ADD) research programme, which will evaluate the use of polygenic risk scores and other tests to identify people at high risk of serious illnesses and new approaches to early detection of disease. The ADD programme will have a cohort of five million people, for whom Genomics plc will provide polygenic risk scores for a number of diseases.

Professor Sir Peter Donnelly FRS, Founder and CEO, Genomics plc, said:
"Professor Sir Mike Richards has recognised the potential of genomic data to ensure earlier detection and treatment of diseases – making a "prevention first" model viable for the first time. Such a model with smarter screening should bring revolutionary benefits to both patients and healthcare systems.

"We are delighted that the UK Government, which has led the world in understanding this potential through the 100,000 Genomes Project, is advancing its belief in the role of genomics in medicine through the Accelerated Diagnosis of Disease programme. We must now fully harness the power of genomic analysis, through the use of polygenic risk scores, to help physicians manage common diseases for the benefit of patients."

About Genomics plc

Genomics plc is a leading genome analysis company formed in 2014 by four leading scientists at the University of Oxford, including Professors Sir Peter Donnelly (then Director of the Wellcome Centre for Human Genetics) and Gil McVean (Director of Oxford's Big Data Institute). Its vision is to use genomic insights to transform drug discovery and precision health.

By amassing and curating data from many sources, Genomics plc has developed the largest engine of its kind in the world linking genetic variants to changes in thousands of measurements and disease outcomes, together with its own breakthrough machine learning algorithms that use this data at scale to discover new drug targets and to predict disease risk to empower predictive prevention.

Backed by some of the leading investors in life sciences, Genomics has an expert cross-disciplinary team of 65 people, primarily scientists and software engineers, with offices in Oxford and Cambridge UK.

For additional information about Genomics plc, please visit www.genomicsplc.com.

About polygenic risk scores

The idea behind polygenic risk scores is to combine information from large numbers (hundreds to millions) of genetic variants carried by a person. Each individual variant typically has only a small effect on a person's risk of developing common diseases. But the impact on risk can become significant when those many small effects are aggregated.

More than a decade of successful large-scale human genetics studies has established that for all the common diseases there are many thousands of genetic variants which contribute to disease risk. Many of these individual risk-SNPs (single nucleotide polymorphisms) are common in the population, but each one typically only has a small effect on risk (<5%). This contrasts with many serious rare diseases where a single, rare, genetic change often has a large effect.

A key practical difference is that to identify the rare mutations which cause rare genetic diseases it is usually essential to sequence, or read, the entire genome of the individual, or the exome (the part which contains the genes). In contrast, the many common variants which affect risk of common diseases can be measured in an individual with a different, and much cheaper, technology using so-called genotyping chips which measure a pre-determined set of ~1 million of the 3 billion positions in the human genome.

For a particular disease or trait, a so-called polygenic risk score (PRS), combines information from large numbers of variants across the genome (hundreds to millions) to give a single numerical score which is an aggregate summary of an individual's propensity to develop that disease on the basis of the DNA variants they have inherited. In principle, polygenic risk scores can be constructed for many diseases – the SNPs involved, and the weightings for them, will typically differ from disease to disease. For an individual, one can thus simultaneously calculate polygenic risk scores for many diseases.

Across a large set of individuals, for a particular trait, there will be a distribution of values for the polygenic risk score. Individuals with higher values of the score will be at higher risk of developing the disease on the basis of the common genetic variants they have inherited.

Depending on the disease, this information could be used by the individual to motivate lifestyle changes, by their doctors to suggest appropriate medical interventions or to help with to diagnosis, or in public health to better target screening programmes.

A critical point is that whilst most individuals will tend to have average risk for any particular disease, it is very likely that they will be at the extreme of genetic risk for *something*. Early identification of these risks, through the availability of genome-wide genetic information, could have a profound effect on individual and population health, and on health-related expenditure. The possibility of generating PRS for many common diseases at a population scale offers the exciting opportunity of identifying individuals in the tail of the risk distribution for a subset of diseases, and to optimise care, prevention, and screening accordingly.

The nature of genetic data means that the population the data comes from can be important. With current approaches, polygenic risk scores tend to be most accurate when they are applied to the same population as the individuals in the genetic study from which they were derived, typically those of European ancestries. A major focus at Genomics plc is to assess the methods carefully in people with ancestries from other parts of the world, and where necessary to improve the methods, and to take advantage of genetic studies underway in different ancestry groups, to produce tools that are equally effective for everyone.

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