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Polygenic risk scores by Roger Watson

What are polygenic risk scores (PGRSs) and why are they relevant to nurses?

Nurses need to know about genetics and most Registered Nurse learns 'the essentials' in an undergraduate curriculum. This is to ensure that they understand, for example, genetic sex determination and the genetic basis of some disorders which they may encounter in their patients. Some nurses go on to work in areas where advanced knowledge of genetics is important. Specialised nurses have long offered genetic counselling to couples where some familial disorders such as haemophilia, sickle cell anaemia and Huntington's disease are present and in communities where consanguineous marriage is common (Salway, Ali, Ratcliffe, Such, Khan, Kingston, Quarrell, 2016; Ali, Salway, Such, Dearden 2018). More recently nurses will work in areas where gene therapies are being developed. However, gene therapies largely remain under development and where nurses work as genetic counsellors, it is mainly with genetic disorders that are well understood in terms of their heritability. Only single gene mutations are present, they are usually recessive and sometimes sex-linked. Therefore, specific advice can be offered about the likelihood of having a child with a genetic disorder and what the likely consequences for the child and the family will be.

But imagine if nurses were able to advise people about their own likelihood—or 'risk'—of developing a disease in later life, based on their whole genome, and what they could do to minimise the risk or adapt to it? This is precisely what PGRSs afford us; a tool in the genomic toolbox which estimates risk of almost any disease provided we have the necessary minimal information about a person's genome. PGRSs are not brand new. However, they are

becoming much more useful due to technological advances which allow rapid genetic sequencing and analysis of very large populations. Based on these definitive samples, increasingly accurate estimates of the likelihood of a particular outcome in an individual are possible.

What is a PGRS?

PGRSs are also referred to as genome-wide polygenic scores and genetic risk scores (Khera, Chaffin, Aragam, Haas, Roselli, Choi, Natarajan, Lander, Lubitz, Ellinor, & Kathiresan, 2018). A PGRS is a value that indicates the likelihood of an outcome developing due to a person's genome. This likelihood is commonly referred to as a 'risk' because PGRSs are usually used to investigate diseases. However, you can have a PGRS for any trait such as height, sporting ability or mental ability (Plomin, van Stumm, 2018). A PGRS accounts for all the genes known to influence a particular outcome and weights some of these according to how strongly they are known to be associated with that outcome (Khera, et al., 2018). PRGSs have increased in popularity and in utility as they are becoming better. Clearly, the more information we have about a trait, the better it can be predicted. Information comes from the samples that already exist; and these samples are becoming bigger. The importance of such large samples—often in the millions—is realised through the existence of, long-standing, longitudinal studies such as the Lothian Birth Cohort Study (http://www.lothianbirthcohort.ed.ac.uk/; accessed 31 March 2019) and the pooling of data from many such large studies, for example, in the UK Biobank study (https://www.ukbiobank.ac.uk/; accessed 31 March 2019).

How it works

From a sample of blood, or by scraping some cells from the inside of the mouth, the genetic profile of an individual can be determined and all factors which are known to be associated with specific outcomes, for example, coronary heart disease (CHD; Knowles & Ashley, 2018), can be identified. Based on the studies of large samples referred to above, the risk of the individual person who has provided the sample developing CHD can be estimated and expressed as a number. The possibilities for scaling up such a procedure are immense as a visit to hospital is not required. Home kits are already available for the provision of samples for genetic testing (https://www.health.harvard.edu/newsletter_article/direct-to-consumer-genetic-testing-kits; accessed 31 March 2019) and these could be ordered and returned to a laboratory specialising in PGRSs and the results returned to you. Clearly there may have to be subsequent follow-up with expert clinicians (including appropriately educated nurses) and an understanding conveyed that such tests and the values of PGRSs obtained are neither diagnostic nor predictive—merely indicative. Based on a person's PGRS advice could be provided about what the score means, and from an evidence-based perspective, appropriate advice could be provided. Using CHD as an example, advice about smoking, body weight and exercise would be relevant. Of course, such advice is relevant and helpful to anyone; but they are more likely to listen if they have some evidence that they are at higher risk.

What we know

In theory, there is no limit to what can be estimated using PGRSs but some specific examples of PGRSs for non-communicable diseases (NCDs) including CHD, type-2 diabetes, inflammatory disease and breast cancer exist (Khera, et al., 2018). While the potential for a low-cost method of indicating risk and providing health professionals with a useful starting point for individualised health promotion, PGRSs remain untested clinically (Knowles, & Ashley, 2018). Ideally clinical trials studying their implementation with measurable health

outcomes would be ideal; but given the length of time between genetic testing and the development of NCDs, this is likely to take decades to achieve. Also, there is criticism that PGRSs—largely generated from Caucasian samples—may not apply across other ethnic groups (Khera, et al., 2018).

Nevertheless, it is not inconceivable that PGRSs could be generated for a wider range of ethnic groups and that they could be tested robustly. Given the evidence for their potential, their increasing accuracy and the ease with which an individual's PGRS can be obtained, they are likely to become incorporated into clinical practice, especially in preventive medicine and health promotion. On the other hand, the ease with which genetic testing can be done, the natural concern that people have for their health and the widespread existence of medical charlatans who—playing on people's concerns—may use this to peddle expensive, ineffective and possibly dangerous 'remedies'. All the more reason for educated health professionals—with nurses at the forefront—to be knowledgeable about PGRSs and to be prepared to counsel patients and conduct their own research.

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