EDITORIAL

The utility of population level genomic research

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The final issue of EJHG for 2022 takes in research from the individual to population level and back again. Hastings Ward and colleagues from Genomics England open with a thought provoking piece on how best to engage patients and their families with genomics research [1]. There is clear scope for participants to help shape and develop research, rather than being passive sources of data. Research projects must not only be sensitive to participants but reflect the needs of researchers. Klinger et al. report a survey of users of biobanks [2]. Many reported not using resources from biobanks, citing a variety of reasons such as cost. This calls into question the sustainability of biobanks.

Biobanks facilitate population genetic studies. Studying populations is immensely valuable for both the science and clinical practice of genetics. An Australian study of population incidence of Duchenne muscular dystrophy did not demonstrate any reduction in incidence despite increasing genetic services [3]. This has implications for service design. Hay et al. use the UK biobank data to investigate the role of PCSK9 in human disease, demonstrating a potential impact on mood and cardiovascular risk factors from variants in this gene [4]. Population level data can also help us understand clinical phenotypes better. Doser et al. report that for Danish school children, a diagnosis of neurofibromatosis type 1 is associated with lower exam grades [5]. Sufficient power to demonstrate this would likely only be achieved with a nation wide dataset. Watkins and colleagues use a large population DNA dataset to demonstrate a potential effect of grandmaternal smoking on DNA methylation in grandchildren [6]. This has obvious public health implications. Meaningful data on rare diseases can, by definition, only be obtained from large datasets. Tubulointerstitial kidney disease have few diagnostic/defining clinical or histological features. Popp et al. used the German Chronic Kidney Disease dataset to dissect the genomic basis of this unusual kidney condition with implications for diagnosis [7]. Population studies can also assist with genomic diagnostics: Morena-Ruiz et al. present a paper describing a model to identify digenic causes of disease [8]. Studying populations of rare disease patients also helps us understand common diseases, Boot et al. write an interesting comment on common movement disorders in 22q11 deletion syndrome [9]. Recruiting and retaining participants to these large population studies poses a number of practical and ethical challenges. The Cooperative Health Research in South Tyrol (CHRIS) study reports a novel, dynamic consent model to address some of these issues [10].

At the level of the individual patient, exome and genome sequencing have clear clinical utility. However, precise measures of benefit and utility for these tests are underdeveloped. Hayeems et al. present further evidence to validate the Clinician-reported Genetic testing Utility InDEx (C-GUIDE), which may be used in studies to investigate perceived utility of genomic testing [11]. What is clear, is the unease over the potential lack of utility of direct to consumer testing. Martins et al. provide an updated review on ethical issues and clinical concerns around direct to consumer testing [12].

In many nations, genomic testing is provided by a multidisciplinary team. However, there is inconsistency in the role and training of genetic counsellors. Catapano et al. report a European survey of how geneticists perceive the role of genetic counsellors [13]. Medical Geneticists clearly valued the role of a Genetic Counsellor within their team, recognising their unique skills. For example, the skills of a Genetic Counsellor would be required when discussing prenatal findings of a rare trisomy detected by non-invasive testing, with the affected couple [14, 15].

We most not forget that with the vast expansion in genomic testing, happening across the globe and in a variety of settings (clinical, academic, industry et al), there remain real concerns about genetic discrimination. Joly and Dalpe provide a timely commentary on this [16].

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ADDITIONAL INFORMATION

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