Abstract Title: From Genetics to Genomics: lessons from the DDD and 100,000 Genomes projects, UK Biobank and the National Disease Registration Service

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Abstract: The UK has been at the forefront of translating discovery of DNA structure into genomic knowledge beneficial to population health. We began with rare syndromes in the DDD project www.ddduk.org which pooled child parent trios presenting to genetics services. Their focus on exomes gave way to a push to primary use of whole genome sequencing in the 100,000 genomes project in families with a range of phenotypes and cancer. Under government owned "spinout", Genomics England (GEL) www.genomicsengland.co.uk the target was achieved in 2018. The team have gone on to develop a range of resources such as the sequencing of 20,000 people affected by Covid 19 and 15,000 controls to understand predisposition. This supported the identification of an HLA type common in Northern latitudes which offers resistance to Covid induced illness.

As high volume sequencing became established, the samples banked from the 500,000 people in the UK Biobank www.ukbiobank.ac.uk between 2006 and 2010 have been used to develop an unparalleled 'omic data resource from an unselected group of people aged 45-69 at recruitment. By 2021, the annual list of publications had exceeded a thousand.

A significant drawback of UK Biobank is the lack of ethnic diversity. GEL has launched a Diversity initiative to help address this deficit. GEL also has a Cancer 2.0 project addressing the value of long read sequencing together with pooled 'omic data sets. The next challenge is the sequencing of 100,000 newborn babies to identify the early onset high penetrance genetic disorders.

My personal focus has been on the common hereditary cancer disorder, Lynch syndrome. Our National Disease Registration Service now tracks over 9000 cases to ensure effective surveillance. Interpretation of variants remains a general diagnostic challenge. Global efforts include our www.brcaexchange.org project containing over 70,000 variants in BRCA1&2 as a model for future international collaboration.

Area of expertise: Clinical Genetics, cancer genomics cancer prevention