Project title: Longitudinal analyses in patients with inherited genetic susceptibility: real-world data science meets early detection/prevention of cancer.

Project Summary:

Project: Working with the supervisory team, the applicant will develop a project application involving longitudinal analyses examining associations and outcomes for individuals with genetic susceptibility to cancer. This will involve data linkages using the newly-established 'National Inherited Cancer Predisposition Register' (NICPR); the specifics of the project will be focused on genetic susceptibility syndrome(s) and cancer(s) reflecting the applicant's interests.
With full historic amalgamation as well as real time prospective registrations, the NICPR constitutes a single central dynamic live register of all CSG GPV-carriers nationally. Due to internationally ubiquitous issues relating to data governance, incompatibility of data-systems and data formats, no other country has yet been able to achieve this. Meaning the NICPR is a world-first. Most importantly, the NICPR is: (i) inclusive and representative (ie not biased by research-willing participants); (ii) pan-gene (where research studies to date have focused on specific gene(s)); (iii) longitudinally comprehensive (with complete records on genetic testing back to the 1990s and cancers dating back to 1980s).
Held in the National Disease Registration Service (NDRS) alongside multiple other nationally-collected NDRS-held datasets including cancer registrations, pathology, hospital and GP episodes, prescriptions, chemo and radiotherapy administration, individual-level data linkage of the NICPR will allow us for the first time to address important questions about risk, cancer management, survivorship and outcomes in cancer patients with inherited germline pathogenic variants (GPVs). What are the differences in cancer risks, treatments and outcomes for individuals with GPVs? How do the risks of second cancers differ from individuals with a sporadic cancer? What is the uptake/impact of risk reducing surgery, chemoprevention and intensive surveillance regimens? What are the impacts on non-cancer outcomes of a genetic diagnosis?
Given the incipient dramatic expansion in genetic testing at cancer diagnosis and more broadly (as per the NHS 10 Year Plan), focus on the clinical trajectory for patients with GPVs is long overdue: inception of the NICPR will allow us for the first time to address these questions via large-scale longitudinal data-driven approaches.

Fellowship: Whilst existing skills in data analysis and statistics would be an advantage, this is not a requisite and we would support the fellow in undertaking the prestigious 3-week Advanced Course in Epidemiological Analysis at the London School of Hygiene and Tropical Medicine in which the basics of epidemiology, statistics and programming in STATA/R are well taught. The post would be based at ICR (Sutton) in the Turnbull team, benefitting from exposure to a broad range of genetics-related projects underway in the Turnbull team (eg related to genomic variant interpretation (CanVIG-UK, CG-MAVES) and BRCA-DIRECT) and more broadly within the Division of Genetics and Epidemiology. We are happy to consider flexible working arrangements.

Supervisory Team:

- Professor Clare Turnbull (Clinical Geneticist, Genetic Epidemiologist, Division of Genetics and Epidemiology, ICR)
- Professor Amanda Cross (Cancer Epidemiologist, Imperial School of Public Health and the Department of Surgery & Cancer, Imperial)

The project and fellow will also benefit from detailed input and supervision from the NICPR national research advisory committee, comprising Dr Steven Hardy (Lead for Genomics, NDRS, NHSE),

Professor Marc Tischkowitz (Professor in Medical Genetics, University of Cambridge), Dr Helen Hanson (Reader in Medical Genetics, University of Exeter) and Dr Fiona Lalloo (Lead of Clinical Cancer Genetics, Manchester Foundation Hospitals). Working closely with co-investigators Hardy, Tischkowitz, Hanson and Lalloo, Turnbull led the Cancer Research UK (CRUK) catalyst award CanGene-CanVar (2019-2025, https://www.cangene-canvaruk.org/), through which the data architecture and information governance for centralized national lab genomic data submissions were established and upon which the NICPR has been developed; accordingly the supervisory team have extensive experience in the management and analysis of these types of data.

Clinical Specialities:

Clinical Genetics, Public Health, Pathology, Oncology.