Project Details	
Project Code	MRC22PHSEx Thirlwell
Title	Improving cancer risk stratification using population based patient characteristics and cancer genotype.
Research Theme	Population Health Sciences
Summary	Cancer and chronic illness pose an enormous burden on population health, leading to demand on NHS services and socioeconomic cost. Genomic analysis of cancer to guide personalised therapy is now routine. There is an increased risk of developing cancer when other clinical diagnoses or anomalies in routine blood tests are present. This project will investigate the molecular profile of cancers analysed in routine care and determine the impact of chronic illness.
Description	Background: One in two people born after 1960 will be diagnosed with cancer. UK cancer outcomes fall behind other European countries. Alongside national differences in cancer outcomes, there are also regional differences in the UK. Approximately 75% of cancer patients have one or more chronic medical conditions (also known as multimorbidity). This is very relevant in the South West of England where there is an ageing population. Prof Hamilton's group has previously identified a link between raised glucose or raised platelet counts measured in primary care and an increased risk of developing/harbouring cancer, including colorectal (CRC) and lung cancers. There is also an increased risk of developing certain cancers (including CRC) in people living with type 2 diabetes (T2D) and obesity. To date, no-one has investigated the distinct genomic profiling of CRC and lung cancer in patients with associated raised glucose and /or platelets. This may identify novel molecular sub-groups of cancer, new therapeutic targets and, in the future improve screening and risk stratification, prognostication and bespoke follow-up regimens. This PhD project will be embedded in a larger on-going research programme run collaboratively by the co-supervisory team. Oncology is an exemplar of utilising personalised medicine to guide treatment. The 100,000 Genomes Project was delivered as a transformation project across the NHS and was the largest undertaking of whole genome sequencing (WGS) globally in routine clinical care. Analysis of the cancer arm of 100,000 genomes legacy data has shown that whole genome sequencing identified a potential therapeutic target or clinical trial in 50% of cancer cases. Due to these findings, cancer patients' tumours now routinely undergo genomic analyses as part of NHS standard care. This involves targeted panel testing of 500 cancer-related genes to guide treatment and aid prognostication. In the South West, gene panel analysis will be performed in the SW Genomic Laboratory Hub (GLH). This studentship will address a significant gap in cancer genomics and population health research and will directly inform clinical practice using established and novel statistical and bioinformatic techniques applied to large healthcare datasets. Proposed approach: The South West GLH will analyse 10,000 cancers over the first two years of the project, including an estimated 1000 CRC and 1300 lung cancers. The student will study at the South West Genomic Laboratory Hub (Prof Rachel Butler is Operational Director) and University of Exeter. They will be trained to analyse and interpret cancer genomic variants, working alongside NHS

	Clinical Scientists. These data will be integrated with primary and secondary care clinical data under the supervision of Prof Chrissie Thirlwell (Clinical Director SW Genomic Medicine Service Alliance), Prof Willie Hamilton (Primary Care cancer risk). The student will benefit from collaboration with the Institute of Data Science and Artificial Intelligence (IDSAI Exeter) and the Translational Research Exchange at Exeter (TREE). The aims of the project are to: 1: Integrate cancer phenotype, genotype and clinical data for individual patients; including multimorbidity, exposure to risk factors, socio-economic (assigned by postcode), and adherence to screening. 2: Determine which genes are mutated and which biological pathways are important in CRC and lung cancer development associated with raised glucose and platelet count. This will be the first study to investigate cancer genotype in the context of comorbid phenotypes eg type 2 diabetes and obesity. It will also determine common co-morbidities and excess risk in the South West cancer patient population. This findings from this project will be used in the future to improve cancer screening strategy, risk stratification and overall population health.
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