their confirmed genetic diagnosis. Through behaviour change approaches, encouragement and motivation the CNS facilitates lifestyle interventions by setting achievable goals. Continued education underpins the young person's knowledge of FH and its optimal treatment enabling them to make informed consent with regards to their future management.
Our mission is to develop a dedicated young person's clinic for FH which will allow young people to feel in control of decision making and confident that their personalised treatment protocol has been designed in collaboration with them. We believe that if a young person feels involved in decisions regarding their care and management that they are more likely to adhere to the treatment protocols which have been recommended.

LIPOPROTEIN PHOSPHOLIPASE A2, HIGH SENSITIVITY C REACTIVE PROTEIN AND CAROTID INTIMA MEDIA THICKNESS IN CARDIOVASCULAR RISK ASSESSMENT FOR A SOUTH ASIAN POPULATION

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South Asians (SAs) in the UK have a higher cardiovascular disease (CVD) burden. Established risk factors predict atherosclerotic risk but not plaque rupture. We evaluated the relationship between Lipoprotein associated phospholipase A2 (Lp-PLA2) activity, a marker of plaque rupture, high sensitivity C-reactive protein (hsCRP), carotid intima media thickness (cIMT) and aortic pulse wave velocity (aoPWV) and the traditional CVD risk factors in SAs.

SAs (n = 106; aged 30–75 years, females 53%) from a temple-based CVD screening programme who were statin naïve and non-diabetic were recruited. Medical history, blood pressure, anthropometry, body fat analysis, blood tests, CVD risk assessment (Joint British Societies'2 (JBS2), cIMT and aoPWV were carried out.
Univariate correlations for Lp-PLA2 were significant with low density lipoprotein cholesterol (LDL-C) ($r = 0.26$, $p = 0.01$), HDL-C ($r = -0.27$, $p = 0.005$), non-HDL-C ($r = 0.31$, $p = 0.002$), total cholesterol (TC) ($r = 0.20$, $p = 0.048$) and triglycerides (TGs) ($r = 0.22$, $p = 0.02$) but not with cIMT or aoPWV. After adjusting for HDL-C, TC and TGs, LDL-C shows a trend of independent association with Lp-PLA2 activity ($p = 0.06$). hsCRP levels correlated with waist circumference ($r = 0.23$, $p = 0.02$) and body mass index (BMI) ($r = 0.24$, $p = 0.02$) but no other variables.
Mean Lp-PLA2 activity and cIMT, but not hsCRP, increased sequentially in low, intermediate and high risk groups but was only significant for cIMT. Mean (SD) cIMT on the right (R) and left (L) were 0.54 (0.09) mm and 0.55 (0.11) mm respectively and different ($p = 0.028$) Bilateral mean cIMT increased sequentially and significantly in low, intermediate and high CVD risk categories ($p = 0.0014$ and $p < 0.0001$ for L cIMT and $p = 0.0045$ and $p = 0.0005$ for R cIMT; intermediate and high CVD risk categories compared with the low CVD risk category).
Lp-PLA2 activity and cIMT may be useful for further risk stratification in addition to traditional risk factors in this population with a high CVD burden

DEVELOPMENT OF A REGIONAL FAMILIAL HYPERCHOLESTEROLAEMIA (FH) GENETIC CASCADE TESTING SERVICE FOR THE NORTH OF ENGLAND

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In April 2014 The Northern England Strategic Clinical Network Lipid Advisory Group secured the support of the Northern CCG Forum and funding from the British Heart Foundation (BHF) for two nurses and one administrator to enable the establishment of a region-wide Familial Hypercholesterolaemia (FH) Genetic Cascade Testing Service.

The Northern Clinical Commissioning Groups Forum (13 CCGs) agreed to provide funding for first year family cascade tests and the full service costs once the BHF and AHSN funding was finished. Working closely with the Forum it was agreed that patients would be referred for genetic diagnosis if they had Dutch Lipid Clinic Network (DLNC) Score of greater than 5 and at least 2 relatives eligible for cascade testing.
The Northern Genetic Service in collaboration with NewGene, with Academic Health Science Network (AHSN) funding, developed a bespoke two-tier "chip and sequence" genetic testing strategy incorporating mutations frequently found in the North East in the first tier followed by a next generation sequencing assay in the second tier for those probands with a negative first tier result.
The majority of trusts across the network have well established lipid clinics and the adult and paediatric clinicians work closely via the Lipid Advisory Group. Cases are discussed in regular Regional FH Multidisciplinary Team meetings. The FH Cascade Testing Specialist Nurses are hosted by a single NHS Trust (City Hospitals Sunderland) and will work closely with specialists across the network and manage their workflow using PASS Clinical® licences funded by Astra Zeneca.
The NIHR Diagnostic Evidence Co-operative Newcastle (DEC) will assist in the evaluation of the project's impacts on activities, costs, and patient and population benefits.
The future success of the programme will require promotion of awareness of the service and collaboration with GPs to help them identify and refer their FH patients to the lipid clinics.

ASSESSMENT AND INTERPRETATION OF VARIANTS OF UNCERTAIN SIGNIFICANCE (VUS) IN FAMILIAL HYPERCHOLESTEROLAEMIA

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The Bristol Genetics Laboratory uses Next Generation Sequencing (NGS) technology to identify variants in the genes known to cause autosomal dominant familial hypercholesterolaemia (FH) (*LDLR, APOB, PCSK9*).Variant interpretation and classification is performed using a repertoire of software and online tools, including Alamut, to obtain population frequency data, splicing predictions and predictions of amino acid substitution on protein function. This information is used in conjunction with comprehensive literature searches and correspondence with other UK FH testing laboratories to determine whether the variant is likely to be pathogenic or a benign polymorphism.

Since September 2013, over 1000 samples have been tested and around 6% of patients have been reported as having a variant of uncertain significance (VUS), where pathogenicity cannot be elucidated through our current methods. In order to further classify these variants, segregation analysis is often required. The key benefit of classifying these variants is the ability to activate genetic cascade testing for relatives.
Recently, 12 LDL-C-raising SNPs have been identified across the genome (Talmud et al, 2014, *The Lancet*). Individuals who carry multiple LDL-C SNPs have an increased likelihood of having LDL-C concentrations above the diagnostic threshold for FH (polygenic FH). The NGS assay has been redesigned to incorporate these SNPs as a further tool in the interpretation of VUS; a VUS having a higher likelihood of pathogenicity in patients with a low LDL-SNP score.
The additional LDL-SNP score will be used alongside updated bioinformatics searches, including ExAC, to gain additional population frequency data and data sharing amongst the FH testing laboratories to potentially reclassify the 6% of patients with a VUS previously identified in the laboratory. Data and interesting case studies will be presented.