HEALTH INNOVATION
North West Coast

NHS

Genetic hypercholesterolaemia and lipoprotein(a) – a call to better assess cardiovascular risk

JUNE 2026

HEALTH INNOVATION North West Coast

NHS

This paper provides an overview of current testing capabilities for monogenic and polygenic hypercholesterolaemia and lipoprotein(a) across the North West of England. It highlights challenges, opportunities, and practical steps to improve detection of familial hypercholesterolaemia (FH) and related conditions, ultimately aiming to reduce cardiovascular disease (CVD) risk.

EXECUTIVE SUMMARY

Familial hypercholesterolaemia (FH) is a common inherited condition with a high risk of premature CVD yet remains largely undiagnosed. In the North West an estimated 29,200 individuals have FH. Generally, fewer than 10 per cent of those with this inherited condition are diagnosed[1]. Despite recent increases in testing, the current pace of identification means full detection would take several decades, significantly limiting prevention impact.

Lipoprotein(a) [Lp(a)] is an important genetically determined CVD risk factor, but testing is not routinely commissioned by the NHS and is not included in the national genomic test directory[2]. As a result, Lp(a) related risk is largely unrecognised in current pathways, despite growing (inter) national support for once-in-a-lifetime measurement in higher risk individuals.

Genomic innovation offers a major opportunity to improve detection and risk stratification, combining monogenic FH testing with polygenic risk and Lp(a) assessment, supported by digital tools and alternative sample collection methods. The North West is well placed to lead this agenda, with available genomic laboratory capacity, established regional infrastructure, and emerging local pathways that could accelerate equitable CVD prevention at scale.

Paper by Theun van Veen, Project Manager at Health Innovation North West Coast Patient Safety and Care Improvement Team

CURRENT STATUS

FH is a genetic disorder that causes very high cholesterol and significantly increases the risk of premature coronary artery disease and stroke. Despite its impact, most affected individuals remain undiagnosed – national estimates suggest only 10-15 per cent are identified. Genetic testing is the gold standard for FH diagnosis and is delivered through seven NHS Genomic Laboratory Hubs (GLHs) across England.

The North West Genomic Medicine Service Alliance (NW GMSA) collaborates with NHS teams, Integrated Care Systems, pathology networks, and cancer alliances to embed genomics into routine care. However, structural and capacity challenges persist, limiting progress toward diagnosis and prevention goals. Specialist lipid clinics triage patients for genetic testing eligibility. In the North West, samples are typically processed by the Manchester-led North West GLH.

Beyond FH, there are other hereditary conditions that also cause raised cholesterol levels such as polygenic hypercholesterolaemia and raised Lp(a). In recent years these conditions have been getting more attention as they are acknowledged as important risk factors for CVD. While commercial tests are available, testing is not routinely offered via the NHS and it is not available across the board.

SCALE OF THE CHALLENGE

The North West population of 7.3 million includes an estimated 29,200 individuals with FH; it affects one in 250 individuals in the UK. Fewer than 10 per cent (<2,920) have been diagnosed. Between November 2023 and March 2025, 3,750 patients were tested, with an estimated 15-20 per cent positive rate (562-750 confirmed FH cases)[3]. At this pace, full identification would take nearly 40 years.

While the NHS Health Check targets eligible adults aged 40-74 years old to support CVD risk reduction, the challenge remains to (routinely) identify younger individuals (<40) whose elevated risk is driven by inherited lipid disorders.

10 YEAR HEALTH PLAN FOR ENGLAND

Under the updated **10 Year Health Plan for England**, as part of the prevention strategy, there is a longer-term plan to create an entirely new prevention paradigm within the NHS: genomics and predictive analysis to benefit population health. There is commitment to expand genomic testing for inherited causes of major diseases to allow earlier detection and intervention, which includes CVD predisposition (e.g. FH). The time is now to capitalise on this renewed commitment for England to prevent premature death from CVD.

CURRENT PRACTICE

Distinguishing FH from common forms of hyperlipidaemia can be complex.

- The commissioned test for **FH** currently includes analysis of variants in one of the following five genes: APOB, APOE, LDLR, LDLRAP1 and PCSK9.
- In contrast to monogenic FH, **polygenic hypercholesterolaemia** results from the cumulative effect of multiple common genetic variants that modestly raise LDL-cholesterol. Individuals may present with LDL-C levels overlapping with FH, making differentiation challenging without genetic testing. Around one in 20 to one in 100 people have polygenic hypercholesterolaemia[4]. It can lead to slightly or moderately raised cholesterol, with very high cholesterol classed as severe – the latter can look like FH but the cause is different, as many genes are involved.
- **Lp(a)** is made of a lipoprotein similar to LDL plus two proteins known as ApoB and Apo(a). The amount of Lp(a) in the blood is determined by genes. Around one in five people are at high risk for atherosclerotic CVD and aortic valve stenosis due to high Lp(a) levels[5].

While diagnostic criteria for FH are well established (e.g., Simon Broome, Dutch Lipid Clinic Network), only patients meeting these criteria are tested. Blood samples are preferred for genetic analysis, though saliva is an alternative – especially for children or where phlebotomy access is limited. Cascade testing of relatives is recommended after an FH diagnosis, but capacity constraints often limit implementation.

Patients testing negative for FH may have other genetic lipid disorders, yet polygenic hypercholesterolaemia and Lp(a) testing are not currently commissioned by the NHS, though commercial options exist and there are examples of NHS services that have integrated these (commercial) options into existing pathways.

INNOVATION

HEALTH INNOVATION NETWORK (HIN)

Previously, FH was a clinical workstream which formed part of the Health Innovation Network's CVD Portfolio Programme. GENinCode, a company with expertise in genetic testing which includes FH, has been identified through the work of the CVD Clinical Working Group as a company with innovations to support earlier diagnosis and treatment of high-risk cardiovascular conditions such as FH.

Under our remit to support the adoption and spread of innovation, the CVD team has been exploring the feasibility of innovations such as GENinCode being implemented into diagnostic pathways for FH in the North West of England.

FROM PILOT TO BUSINESS AS USUAL

Health Innovation North East and North Cumbria (NENC) supported pilots to improve access to FH genetic testing. Specifically, objectives were focused on acceptability of LIPID inCode testing in secondary care, to offer direct testing to help reduce waiting lists for those patients who were referred as 'questionable FH' in secondary care and direct testing of those at risk of FH who were identified from primary care searches. Results from a baseline audit explored clinician and patient experience with the testing technology LIPID inCode® provided by GENinCode PLC, a commercial FH test which provides an alternative to the current service delivered via the GLHs. LIPID inCode® is a genetic test provided by GENinCode for the diagnosis of FH with further coronary risk stratification of the patient. Both blood and saliva samples can be used for testing. This test assesses the probability of polygenic hypercholesterolaemia and genetic coronary risk, as well as pharmacogenetics of statins and predisposition to elevated Lp(a). This aligns to regional and local CVD prevention strategies.

The outcome has been successful delivery of the objectives and the LIPID inCode® test was implemented in the north of England in Newcastle, Leeds and Sheffield. The driver for this change was in part capacity challenges around genetic testing for FH at the North East and Yorkshire NHS Genomic Laboratory Hub (NEY GLH).

The NEY GLH has drawn in resources for FH genetic testing by implementing LIPID inCode® testing, to also aid faster turnaround times and delivery at lower cost than the NHS. As a result, it has potential to release NHS/GLH expertise and capacity to prioritise other areas of genetic testing. **Read the full pilot study report here.**

LP(A)

International guidelines increasingly recommend once-in-a-lifetime measurement of Lp(a), particularly in individuals with premature CVD, FH, or a family history of early coronary disease[6]. In 2025, HEARTUK put out a joint paper with The Association for Laboratory Medicine on standardising lipid testing and reporting in the UK and recommend including Lp(a) with other cholesterol tests for high-risk patient to enable improved CVD risk-scoring. While no specific Lp(a)-lowering pharmacological treatment is available at present – a number of **trials evaluating Lp(a) specific lowering therapies** are under way or completed – the **paper references a calculator** to support clinicians with more accurate risk stratification, enabling more intensive management of modifiable factors. Emerging health economic data also suggest that Lp(a) testing is already cost-effective through improved cardiovascular risk stratification and optimisation of existing preventive therapies, with potential to reduce future cardiovascular events[7].

MAINSTREAMING ACCESS TO GENETIC TESTING AND CVD RISK SCORING

DNA samples for genetic testing can be obtained from blood, saliva, or cheek swabs, with blood providing the highest quality. Triaging requires lipid profile results, emphasizing the need for widespread lipid screening. Ideally, all adults should have a lipid profile as part of NHS prevention strategies, enabling targeted genetic testing and cascade screening for relatives. For any approach, equity of access will need to be ensured.

DIGITAL

NHS mobile apps should have a role in collecting information directly from the patient so support triaging. This would empower patients. This should be supported by digital regional teams who are given a clinical remit as part of this commissioning, ideally existing experienced teams provided with increased capacity, who can direct the appropriate follow-up for the patient, linking in local clinics and/or healthcare providers.

Case-finding tools/algorithms have been trialled to help find patients using healthcare records. However, to date this has often been confined to a localised (pilot) project[8,9]. While useful, to be most effective, these tools need to be employed at a larger scale, where ideally lipid profiles for patients are also available. Furthermore, any approach will need to encompass pedigree testing.

COMMUNITY

Community pharmacy lipid testing and NHS Health Check programmes may provide opportunities to identify individuals with markedly elevated LDL-C requiring further genetic assessment. In addition, the **10 Year Health Plan for England** outlines how the new Neighbourhood Health Service will bring care into local communities, convene professionals into patient-centred teams and end fragmentation. These neighbourhood teams can really take a role in engaging hard-to-reach demographic groups, whether these are specific age groups, or specific populations who are less likely to engage with health care teams for a variety of reasons, such as not being eligible for the NHS Health Check. More importantly, as this aligns GP practices with social, community and voluntary services, there will be a need within the primary care setting for dedicated funding and capacity, extended to phlebotomy and laboratory services, education covering these conditions, and clear lines of responsibility across the system about how to act on such test results.

This community work starts with engagement and a lipid profile to help understand who is most at risk of premature CVD – local teams are best placed to understand the local neighbourhoods and have a role to play in the NHS prevention strategy.

PROVIDING SAMPLES FOR TESTING

While blood samples are preferred for genetic testing, access to phlebotomy services is not always straightforward and blood collection can be difficult for children or individuals with needle phobias, for example. Using saliva is non-invasive and painless, making it easier and less stressful to collect. In addition, people can use saliva kits in their own home, or they can be used in areas where there is no/limited access to phlebotomy skilled staff. Community-based saliva collection could further improve accessibility.

THE NORTH WEST LANDSCAPE

In contrast to the NEY GLH where there was a capacity challenge that led to commissioning LIPID inCode®, the NW GLH has indicated that there is sufficient capacity to conduct genetic FH testing to meet the current demand, and opportunity to flex capacity should demand increase through proactive case-finding or education. Furthermore, a *'Mainstreaming and Equity: FH Task and Finish Group'* with local stakeholders across the North West has been established to assess the current landscape including barriers to access and support for mainstreaming opportunities while considering data and digital.

The NW GMSA has a responsibility for embedding genomics and genomic medicine within NHS services on an equitable basis. This is undertaken through improvement and transformation of clinical services in partnership with patients and supporting workforce engagement and upskilling in genomics. The recently established NW Genomics Innovation Network, chaired by the NW GMSA Innovation Director, will foster knowledge exchange and collaborative working to accelerate spread and adoption of innovations within genomic medicine and related pathways across sectors and across the North West region.

Regionally, local initiatives are looking to implement pathways around Lp(a). For example, in Lancashire and South Cumbria specialist clinics are exploring a regional pathway on criteria and treatment which will help to bring in a uniform approach. Some Cheshire and Merseyside clinics test all new patients as they see it as important in long-term CVD risk decision-making. Furthermore, local experts are working with national stakeholders – who have linked in with HEARTUK and colleagues in UK-based lipid services – to help standardise Lp(a) testing and management in the NHS.

THE NATIONAL LANDSCAPE

The NHS Genomic Medicine Service enables the NHS to harness the power of genomic technology and science to improve the health of our population and deliver on the commitments in the NHS Long Term Plan. The national genomic test directory for rare and inherited diseases specifies the genomic tests commissioned by the NHS in England. Some tests to assess wider CVD risk are not on the NHS test directory[10]. Previous evaluations indicated that polygenic risk scores to be not clinically effective at that time. Currently testing for Lp(a) is not on the directory. As with increasing evidence-generation, such emerging information will be reviewed.

In April 2025, NHS England (NHSE) and the National Institute for Health and Care Excellence (NICE) published their joint genomic testing pathway[11]. This guidance sets out steps that both organisations have agreed to follow to identify, prioritise and assess new genomic technologies, before they are considered for commissioning by the NHS in England.

NHS Genomic Networks of Excellence were established several years ago, designed to be partnerships between the NHS, academia, the third sector and industry to generate evidence and models of adoption for new technologies and testing, and new discoveries linked to clinical and laboratory practice, in defined topic areas of strategic importance[12]. Recently NHSE published updated guidance for the next phase of the Networks of Excellence – which will run until March 2028[13]. NICE has invited expressions of interest for their continuation and new proposals aligned with the 10 Year Health and Life Sciences Sector Plans. In addition to current themes, NHSE has identified several new areas for inclusion, of which 'integrated risk scores' is one.

Recently, the Genomics Unit and the Health Innovation Network (HIN) have been gathering intelligence to better understand how delivery of NHS England's genomic innovation priorities can be delivered. This also fits well with the 10 Year Health and Life Sciences Sector Plans which both set out a clear focus on genomics.

SUMMARY

Work is taking place regionally and nationally to bring innovations to the genomics ecosystem to ultimately benefit the health of the population. As a system we need to carefully use local intelligence, as well as proven good practice, to share and support the right innovations more widely to improve risk-stratification within the prevention paradigm.

To deliver on prevention goals, the system will need to manage demand and capacity carefully while working towards this new prevention paradigm as outlined in the updated 10 Year Health Plan for England, where genomics and predictive analysis benefit population health. This is especially the case following diagnosis, when the patient will need to be titrated and managed with appropriate lipid-lowering therapies, as well as genetic counselling. To be effective there is a crucial role for education and awareness too, both for patients and for those delivering the services. This all requires capacity and resources planning, and these might not necessarily be available across local health care teams – this requires careful consideration as part of any implementation planning.

Expanding access to FH, polygenic hypercholesterolaemia, and Lp(a) testing – supported by digital tools, community engagement, and innovative pathways underpinned by backing of local and national stakeholders – will be critical to reducing premature CVD across the North West.

KEY RECOMMENDATIONS AND NEXT STEPS

Following the details outlined in this paper, these are our key recommendations on opportunities and practical steps to improve detection of FH and related conditions – such as elevated levels of Lp(a) – to help prevent heart attacks and strokes across the entire population.

- **Expand systematic case-finding for FH,** through wider use of healthcare record–based tools supported by lipid profile data, to enable earlier identification of individuals at high inherited CVD. This should be complemented by **more routine lipid testing in younger populations (<40 years)** to support earlier detection and timely referral for FH genetic assessment.
- **Increase and mainstream access to genetic testing for suspected FH across the North West,** ensuring pathways can scale to meet prevention ambitions.
- **Introduce routine Lp(a) measurement in higher-risk individuals,** aligned with emerging international guidance, to improve cardiovascular risk stratification..
- **Develop integrated, end to end pathways** linking primary care, lipid clinics, genomic laboratory services, digital tools and community settings to support equitable access and timely follow up.
- **Strengthen cascade testing of relatives following an FH diagnosis,** addressing current capacity constraints to maximise the preventive benefit of identifying affected family members earlier. This approach should be extended to relatives of those diagnosed with elevated Lp(a) when this becomes part of routine care.
- **Invest in workforce education, engagement and upskilling in genomics and lipid disorders,** enabling safe and effective delivery of expanded testing and management within routine NHS care.

NEXT STEPS

- Enable future evaluation and adoption of Lp(a)-targeted therapies by strengthening early identification and stratification of inherited lipid-related cardiovascular risk, recognising that Lp(a) testing is not currently routine despite a rapidly advancing therapeutic pipeline.
- Align FH and Lp(a) pathways with national genomics, research and innovation infrastructure, supporting horizon-scanning, evidence-generation and readiness for assessment through established NHS and regional innovation networks.
- Build system and commissioning readiness for emerging therapies, including pathway design across lipid services, genomics and primary care, while maintaining optimised use of existing lipid-lowering treatments during the transition period.

REFERENCES

1. Familial Hypercholesterolaemia, S McErlean et al, BMJ 2023 (382)
2. Digital Genomics Test Directory Service
3. FH Testing Dashboard based on NW GLH Data (NW GMSA) [offline only]
4. Polygenic hypercholesterolaemia, HEARTUK
5. Lipoprotein(a) and cardiovascular disease, B Nordestgaard et al, The Lancet, 2024 (404)
6. 2025 Focused Update of the 2019 ESC/EAS Guidelines for the management of dyslipidaemias
7. Lipoprotein(a) testing for the primary prevention of cardiovascular disease in high-income countries: a cost-effectiveness analysis, J Morton et al, Atherosclerosis, 2025 (409)
8. Pilot to permanent: the FH Hub's success story
9. Improving the identification of patients with a genetic diagnosis of FH in primary care, L Ingoe et al, Atherosclerosis, 2021 (325)
10. National Genomic Test Directory
11. NHSE and NICE Genomic Testing Pathway
12. Genomic Networks of Excellence
13. NHS Genomics Networks of Excellence – Apr'26-Mar'28 phase

CONTACT

Theun van Veen, Project Manager
Health Innovation North West Coast
Vanguard House
Sci-Tech Daresbury
Halton WA4 4AB

@ **info@healthinnovationnwc.nhs.uk**

www.healthinnovationnwc.nhs.uk

Health Innovation North West Coast