Familial hypercholesterolaemia: cascade testing in the UK today

A 2019 review

7%

Only around 7% of people with FH in the UK have been diagnosed.

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Foreword by the British Heart Foundation

I am very pleased to launch this second British Heart Foundation (BHF) report on familial hypercholesterolaemia (FH).

Around a quarter of a million people in the UK – one in 250 of the population – are thought to have FH, an inherited condition that raises blood cholesterol levels and dramatically increases the risk of heart attack or stroke.

Left untreated, FH leads to a greater than 50% risk of heart attack in men by the age of 50 years, and at least a 30% risk in women by the age of 60 years. Yet, early treatment with lipid-lowering drugs can increase life expectancy to near the average.

It is estimated that just 7% of people with FH in the UK are diagnosed, including fewer than 450 of the 56,000 children thought to have the faulty gene.

> **“Only half of England currently has access to genetic testing.**

Parents, siblings and children of people with an FH gene mutation possess a 50% chance of having the condition, yet in England only half of the country currently has access to genetic testing. That’s why the BHF was delighted to see that early detection and management of FH was identified as a priority in the NHS England Long Term Plan, published earlier this year with the ambition of diagnosing 25% of those affected by FH by 2024. While still not perfect, this would be a substantial improvement if achieved.

Over more than 30 years, the BHF has invested in excess of £7 million into bench research led by Professor Steve Humphries. In the 1990s, this research resulted in the identification of the gene mutations that cause FH, and subsequently the development of a highly effective cascade testing model to drive detection and diagnosis.

A further BHF investment of £1.5 million over the past five years into the implementation of cascade testing services across the UK has driven several improvements, including: access to testing, development and improvement of service provision models, education of healthcare professionals and general awareness-raising. As a result, more than 3,500 people have now been diagnosed with an FH gene mutation.

These programmes demonstrate how an evidence-led and joined-up approach can benefit local populations in light of the challenges faced by the NHS, by providing practical and tested solutions that can be adopted at scale.

We encourage commissioners across the NHS to read this report and consider how cascade testing services for FH could be strengthened in their area to enable the remaining 93% – more than 200,000 people in the UK – to access diagnosis and treatments that would greatly improve their chance of a normal life expectancy.

The challenge now is how the health system will respond and deliver on this clear call for action for equitable genetic testing and diagnosis of people affected by FH.

Professor Sir Nilesh Samani
BHF Medical Director

Foreword by Professor Huon Gray

Since the last BHF report was published in 2016, there has been significant progress made in the detection and management of FH thanks to the contributions of a range of partners from across the health, charity and academic sectors.

The importance of detecting those with FH is now better recognised, as is its prevalence (an estimated 1 in 250 of the population). This is supported by new clinical guidelines and implementation support, and guidance to local health and care systems, which has also now been published.

Despite progress, the pathway for the detection and management of high cholesterol is often sub-optimal. The NHS Long Term Plan includes cardiovascular disease (CVD) as a major priority for the next 10 years; emphasising the increasing importance of genomics and setting a clear ambition for the detection of FH. As a result, this is now a clear priority for action at a national, regional and local level.

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> **This is now a clear priority for action.**

This latest BHF report demonstrates examples of progress for which a wide range of partners have played a part. This includes the significant contribution made by BHF through their funding of the FH nurse programme.

As the final phase of funding concludes, it is encouraging to see the impact of this work beginning to be sustained, shared and adopted across local health and care systems. We have a collective challenge to identify more people with FH from GP records, ensure adequate genetic laboratory capacity, detect the additional cases that can be identified using cascade genetic testing of relatives, and do this within a framework of strong information governance.

I welcome this report which addresses many of the challenges and makes helpful recommendations. When undetected or untreated, FH can shorten lives significantly, but with the continued support of all those involved in the diagnosis and management of this condition, and the welcome emphasis on FH in the NHS Long Term Plan, I am confident that progress will be sustained.

I am also greatly indebted to members of the FH steering group who have contributed tirelessly to the progress made to date.

Professor Huon Gray CBE
National Clinical Director for Heart Disease,
NHS England (2013-19), and Consultant Cardiologist,
University Hospital of Southampton

Introduction

Familial hypercholesterolaemia (FH) is a genetic condition affecting approximately 1 in 250 people in the UK, resulting in high cholesterol levels in the blood from childhood and a high risk of early heart disease.[1]

Children have a 50% chance of inheriting the condition if one of their parents has FH. The risk of death from coronary heart disease (CHD) can be significantly higher with FH than without.[2] It is estimated that only 7% of those with FH in the UK have been diagnosed, and only 5% of those in England.

In 2016, the British Heart Foundation (BHF) published a report on a £1.5m, BHF-funded FH genetic testing programme, which piloted the implementation of cascade testing services across the UK.[3] The report outlined the system-level challenges in sustainably embedding FH genetic testing services across the country and in ensuring equity of access. It outlined some key areas for focused effort to support long-term sustainability of these services and highlighted shared themes faced by most of the BHF-funded services, such as:

- variation in service pathways
- use of a national database
- working relationships between multidisciplinary teams
- access to training and education
- cost of service delivery and access to data

Recommendations from the report were taken forward via national forums, in particular the FH National Steering Group, which is a multi-agency group hosted by the BHF and chaired by Professor Huon Gray.

Most of the services have since evolved and the final phase of BHF funding is due for completion in November 2019.

Moreover, there have been changes in external policies and governance structures. These include the establishment of the new national Genetic National Genomic

Medicine Service, sustainability and transformation partnerships (STPs)/integrated care systems (ICSs) in England, and publication of updated National Institute for Health and Care Excellence (NICE) FH clinical guidelines.[4,5] These changes mean that FH services are operating in an evolving healthcare landscape, which has changed substantively over the course of the BHF-programme funding period.

This report provides a current 'lay of the land' synopsis and identifies the barriers that continue to challenge the sustainability of services. It considers whether policy changes have contributed to, or alleviated, pressures on the system. The report aims to serve as a discussion aide to progress the FH agenda within the CVD community.

25%

The NHS Long Term Plan for England has an ambition of diagnosing 25% of those with FH.

Only around 5% are diagnosed in England.

Policy landscape

Despite NICE guidelines published in 2008 and 2017 recommending cascade testing, there has been limited implementation across the UK. This is particularly true in England, where only 50% of people can access cascade testing services.

Cascade testing offers an opportunity to make great strides in diagnosing cases of FH. Economic modelling in the 2008 NICE FH guideline showed it to be a cost-effective intervention if performed widely.[4] Indeed, since the original NICE guideline was published, some statins have come off patent, their costs have markedly reduced and their cost effectiveness has increased.

There have also been advances in DNA testing, further reducing the costs of testing index cases and cascade testing of family members. The success of cascade testing services in Wales and European countries such as the Netherlands, as well as evidence from the BHF-funded programme, provides helpful exemplars for how services could be developed across the UK.[6]

The updated NICE guidelines promote proactive case-finding by searching primary care databases and offering cascade testing. Modelling shows this is highly cost effective, especially when treatment is started early.

Several validated algorithms have been developed to perform this (e.g. the FH primary care case finding and audit tool FAMCAT) and a HEART UK-supported pilot study in Medway, Kent, demonstrated the improvement in identification when a nurse was provided for GP support.[7,8] Although some of the BHF-funded services already undertake this, the systematic search of primary care databases will represent an increase in administrative workload for GP practices, which was costed in the NICE economic modelling. Furthermore, there are limitations on external agencies, such as funded nurses, undertaking this on practices' behalf due to General Data Protection Regulation (GDPR) guidelines.

However, once people at high risk of FH have been identified and assessed, the annual cost will dramatically fall and include only the recurring cost of lipid-lowering therapy (e.g. statins) and annual review. This also enables future generations to be offered a test at the right time.

To delve further into the feasibility of this approach, the FH service in North East England is testing and piloting systematic approaches to searching primary care databases and conducting an economic evaluation. This is being led by the North East Lipid Group, with support from the regional Academic Health Science Network (AHSN), and will go some way to providing guidance to sites looking to adopt proactive case finding.

The BHF commissioned a feasibility study for the development of a CVD Prevention audit that sits across primary care record systems to support case finding of patients with high risk conditions including elevated cholesterol. The study has concluded that such a tool is feasible and development of the CVDprevent audit is now being taken forward in England by NHS Digital, led by the National Clinical Director for CVD Prevention.[9]

From a service provision point of view, an emerging impact of FH guidelines being promoted more widely is that pressures have mounted on services to catch up with unprecedented levels of demand. This has been especially difficult to manage in rural areas and across Scotland, where resources for FH genetic testing are scarce. For instance, some services in Scotland are now running twice as many clinics but don't have the requisite tools and resources to carry on doing that in the foreseeable future.

In England, policy measures in recent years have driven the creation of more integrated approaches to healthcare across the system. Improving detection and treatment of people with high-risk conditions, and the use of genomic tools to do so, have been a particular area of focus.

An FH implementation guide, Familial Hypercholesterolaemia: Implementing a systems approach to detection and management, jointly developed by NICE, Public Health England (PHE), NHS England (NHSE), NHS RightCare, the BHF and HEART UK, was published in 2018.[10] It sets out practical guidance for improvement on diagnosis and treatment of FH to support commissioners and providers with implementation of services.

For instance, Improving outcomes through personalised medicine (2016) sets out the agenda for embedding a personalised medicine approach into mainstream healthcare.[11] Part of this journey is the uptake of genomic diagnostic tools to improve identification of people most at risk of, or predisposed to, developing conditions such as CVD. This has implications for FH testing as this is one of the conditions that could be detected as part of an individual's holistic review.

In fact, FH was recently cited as an exemplar of how genomic technologies can be embedded into routine patient care, ensuring that early diagnosis leads to effective treatment and direct clinical benefit to individual patients.

Moreover, the NHS RightCare CVD Prevention Pathway refers to FH in the following terms:

- **maintain and improve systematic collection and audit of data on cholesterol levels, high CVD risk and possible FH in practices to support detection and management**
- **achieve local clinical consensus and establish an integrated pathway for detection and management of raised cholesterol and CVD risk.**

A testament to the growing importance of FH is the ambition for 25% of the expected number of people with FH to be identified and optimally managed, as stated in the NHS Long Term Plan for England, published in January 2019.[12] The NHS has committed to deliver this in partnership with the wider system in the next five years. It is crucial that the entire FH pathway is considered to achieve this ambition, ensuring that FH is embedded within the CVD prevention agenda to address issues in its implementation, including ethics, counselling, training and data provision.

There are also discussions taking place with NHSE to look at the adoption of a central registry with common definitions across the whole pathway (such as the PASS-Clinical database), which could provide consistency in the data capture and referral processes across England. Wales already has a centralised database (PASS-Clinical) and Northern Ireland is in the process of centralising its database (using PASS- Clinical). Scotland, however, has its own independent database. There is consensus that a national database that links up all four nations would be useful.

In December 2015, STPs were announced in NHS planning guidance. NHS organisations, such as hospital trusts, clinical commissioning groups (CCGs) and local authorities came together to develop multi-year plans, taking a 'place-based approach' for the future of health and care services in their area. Whether this change has resulted in any impact on areas planning for FH genetic testing is largely unclear. However, this seems like another sensible platform through which to address service provision across a larger geography.

One example of an STP area having a positive impact on equity of access is from Frimley Health and Care STP (see case study box).

Case study: Frimley Health and Care STP

There are three CCGs in Frimley Health and Care STP and they have a group working to reduce variation and improve CVD care.

Surrey Heath was the only CCG in the STP that did not have access to an FH cascade service. East Berkshire CCG is covered by a current BHF-funded project from the Royal Brompton and Harefield NHS Foundation Trust. North East Hampshire and Farnham CCG commissions the Wessex Clinical Genetics Service, which was a BHF-funded FH early implementer site.

The STP reviewed the options in the area and as a result, from April 2018, Surrey Heath joined the Hampshire CCGs in commissioning a service from the Wessex Clinical Genetics Service, providing their population with access to this service.

Similar attempts have been made in other areas. However, it is a difficult subject to broach due to varying priorities and lack of an appropriate forum at which to discuss these challenges.

Some of the problems highlighted stem from the boundary lines of STPs and how they map to CCGs and FH services. North East England, Yorkshire and Humber comprise three STPs. Within the area attention was drawn to one CCG that sits within an STP but is on the border of two distinct geographies where FH services could be delivered. This has created some difficulties in making the case to commission and implement a service for this area. The BHF is convening and facilitating a forum to resolve this and to influence the CCG to sign up for FH service delivery. If this progresses there will be complete access of FH genetic testing to people across North East England, Yorkshire and Humber regions.

This scenario highlights the significant role played by the BHF in influencing decisions by the health system and commissioners. Alongside the evidence from the FH programme, this role has been instrumental in supporting the NHSE decision to move FH genetic testing into specialised commissioning, alongside other inherited conditions. This will take the shape of a National Genomic Medicine Service, operating to common national standards and protocols, and delivering to a single nationalised testing directory.

Genetic testing in labs has also been streamlined with the completion of the recent procurement of genetic testing services in England, resulting in seven centrally commissioned genetic testing laboratory centres. This means that laboratory costs of DNA testing for FH will be covered by the NHS, using standard operating procedures. The 18-month transition, which started in October 2018, is underway, with the expectation that genetic testing will be funded centrally going forward. This should ensure consistency and equity of access across England and is a huge step forward.

Scottish policy is also very supportive of integration and highlights CVD as a major priority. For instance, Better Heart Disease and Stroke Care Action Plan (2009) recommended that a national forum for FH should be established by Scottish Government Health Directorates (SGHD) to raise awareness of FH among primary care professionals; the lipid forum has since met annually. Given the policy horizon in Scotland, FH services have not managed to gain as much traction to sustainably embed a nationally endorsed roll-out model for genetic testing. This is, however, back on the national agenda and being progressed with the National Advisory Committee for Heart Disease. Exploratory discussions are also underway with relevant planning groups and health boards.

It is important that testing for FH is equally available to individuals from all ethnic backgrounds in the UK. While the prevalence of FH in white Europeans has been examined in detail, there is much less data about the prevalence in individuals from the Indian Subcontinent or those of African-Caribbean or East Asian origin. Anecdotally, while people of African-Caribbean origin appear to be under-represented among those attending lipid clinics, individuals from the Indian Subcontinent are well represented, though this is likely to be influenced by referral and deprivation factors.

Genetic studies have identified mutations in UK subjects from the Indian Subcontinent, although as expected the spectrum of mutations is different from White Europeans. UK data on mutations in other ethnic groups is lacking, but current DNA testing methods will be able to identify any mutations present in these individuals. It is possible that, because of cultural and social pressures in different ethnic groups, family-based cascade testing in the relatives of an index case with an FH-causing mutation may require different sensibilities and approaches to be successful, and pilot studies to examine this will be required.

In England, only half of the country has access to genetic testing for FH.

Current service delivery

Following the Welsh FH pilots and the pump-priming of services across the UK by the BHF, there has been a substantive spread of service provision. A five-fold increase in the number of genetically diagnosed FH patients has been reported across the UK since 2010.[13]

The policy landscape continues to evolve, and in some respects is driving the agenda of service provision forward. But despite significant progress around implementation and delivery of services, there are considerable challenges to sustainable service provision for the diagnosis of FH.

Variation in pathways

Several areas are still struggling with differences in service pathways across local geographies. For instance, there are places where the nurse-led model works really well. However, it may not be feasible to implement in areas where specialist FH nurses are difficult to recruit and access to training is limited. This could of course be addressed to some degree by a UK-wide healthcare professional (HCP) training competency programme. Studies such as FAMCAT confirm that nurse-led models reduce the burden on primary care.

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> **Commissioning responsibilities continue to be flagged as an obstacle to consistent service provision in England.**

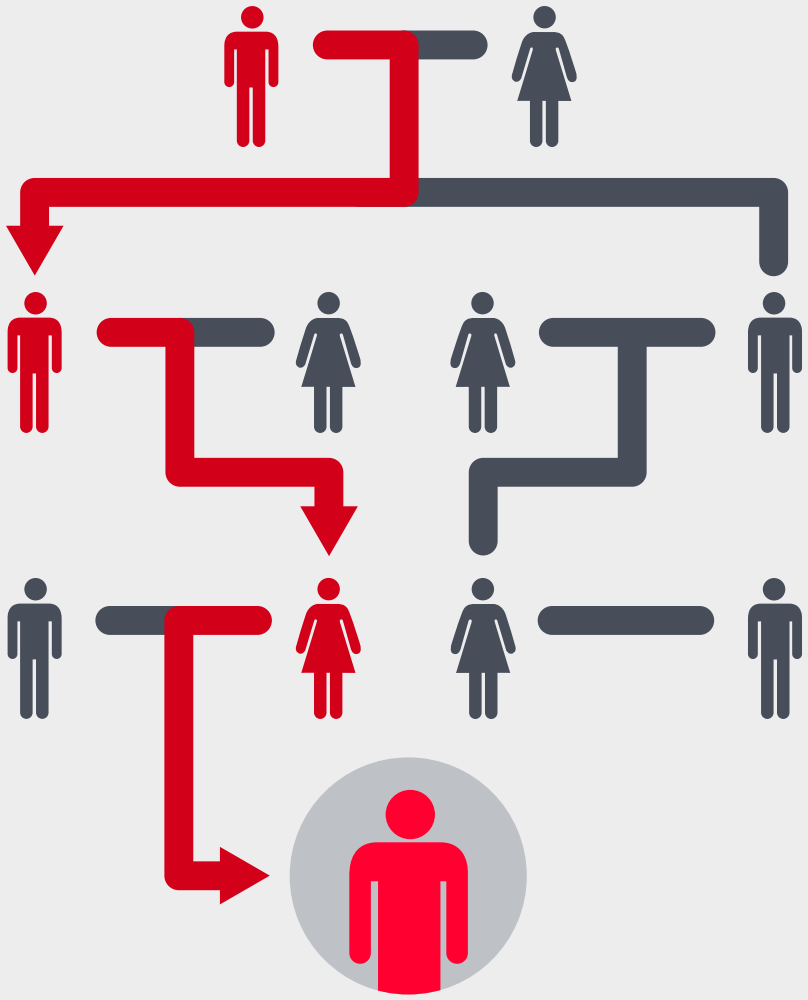
Conversely, areas with lipidologist-led services report bottlenecks and severe strains on services. What appears to be missing is the provision of time and some steer for local services to carry out an evidence-based assessment of current service provision and make decisions to evolve their service models in line with resources and capabilities. As an example, this could involve moving from a lipidologist-led to a nurse led model based on intelligence.

Commissioning responsibilities for genetic testing and for service delivery

The current commissioning responsibilities continue to be flagged as an obstacle to consistent service provision in England. Although the direction of travel is to move

the genetic testing aspect of the FH service to specialised commissioning (in part due to the influencing efforts of the BHF), the service delivery and workforce aspect of services still remain the responsibility of CCGs. A key emerging finding is that FH is not currently considered a priority for a significant number of CCGs and this has implications for whether services need to be subsumed within existing infrastructure: for example, within larger inherited genetic services.

Diagram showing inheritance of the FH genes through generations



There is also a strong drive to outline business cases that are solution-focused and do not have major upfront costs. This has been easier to do at times when working with a consortium of CCGs; for example, within the context of STP planning where resources and capabilities can be shared across CCGs. Connecting the service with ongoing initiatives can also help with securing traction and buy in. For instance, involvement of the West Midlands service with the 100,000 Genomes Project was one of the major selling points of the service.

Overstretched services in Scotland require national direction, as well as national prioritisation of FH as a health need. The increased awareness of NICE guidelines and the work of the FH nurses have led to an increase in relevant referrals in the areas where they have worked. Additionally, their success with case finding and a lack of funding have stretched existing services. The Scottish Lipid Forum is seeking to improve the care for people with FH across Scotland and has formed a steering group for this purpose. A recent application for a national service for FH was turned down but direction has now been clearly given to health boards that FH services should be funded and commissioned at local health board level. Work continues in an attempt to engage in dialogue with Scottish government to prioritise FH services.

The streamlining of genetic testing services into seven Diagnostic Laboratory Hubs has been a positive development for FH genetic testing in England. The new National Genomic Medicine Service will operate to common national standards and protocols, and deliver to a single nationalised testing directory.

Case study: Mainstreaming FH services in Wessex

Created in 2014, the Wessex FH Cascade Testing Service was one of the first FH services to be established in England. It was initially pump-primed by the South Central Cardiovascular Network (SCCVN) and BHF funding to employ two FH specialist nurses. It initially covered a population of 2.6 million across eight CCGs in Hampshire and four in West Berkshire. It has been fully commissioned by these 12 CCGs since 2016. In 2018, the Surrey Heath CCG joined the consortium and Guernsey will be commissioning the service from September 2019.

The service provides clinics in multiple locations and has established specialist paediatric clinics for children in Southampton and Reading under the care of consultants in paediatric endocrinology and FH nurses. Since the launch of the service they have molecularly confirmed FH in over 1,200 probands and over 500 cascades, including children.

Wessex has led the way with economic modelling and has published papers on the quality and cost effectiveness of their model. They currently hold an Health Technology Assessment/National Institute for Health Research £850,000 grant jointly with Professor Nadeem Qureshi of Nottingham University ,evaluating a new protocol for primary care-initiated identification and management of patients with FH, including an observational study and cost-effectiveness analysis.

The 18-month transition started in October 2018. The seven centres will work as a single national service offering any test on the UK Genetic Testing Network Gene Dossier (which includes FH) to a standardised reporting procedure. Simple cases will speed through the system, with a facility within the service to outsource complex variant interpretation to more experienced labs. Once the systems are in place, labs will be able to see other lab reports and how variants are classified. The most significant progress will be to confirm that NHSE will centrally cover final commissioning of genetic testing and associated costs.

Developments in paediatric management and screening

Over the last few years there has been a significant push to provide family and/or child clinics once an index with FH has been identified. However, cascade testing of children is not carried out in a consistent manner across the UK. This is due to the lack of awareness and consideration of the impact; the ambiguity around commissioning/funding arrangements; and lack of skilled/trained staff that are qualified to deal with paediatric cases.

The NICE 2008 guideline includes 37 recommendations on the identification and management of children with FH, particularly that they should be considered for statin treatment by the age of 10 years. NICE also proposed that a UK-wide register should be set up to monitor the long-term safety aspects of early statin treatment. The UK Paediatric FH Register was established in 2012, and has registration and annual follow-up data on over 500 children from more than 60 referring clinicians. Analysis of the data shows no safety concerns and that, in general, children are being treated in accordance with NICE guideline recommendations.

Many services are making good progress in paediatric service provision. Due to a steady increase in service provision, 2018 data revealed that diagnosis for relatives is highest in the under 10's category. This further highlights the importance of consistent provision of paediatric clinics across the country.

- The Wessex cascade testing service was established in 2015 and has a mature paediatric arm in place. This has seen a steady increase in the number of paediatric clinics being run as more children with FH are identified.

- In the West Midlands, the paediatric service recently launched and there are positive early indications in terms of referrals and management.

- In Yorkshire and Humber, the paediatric service is in development. The regional referral centre for the paediatric service is Sheffield Teaching Hospital. Hull University Teaching Hospitals NHS Trust is working together with Leeds, York, Calderdale and Huddersfield to develop a paediatric service where patients can be seen either in joint family clinics or a paediatric clinic, held monthly. It is, however, proving to be more difficult in this region due to a lack of paediatric resource and interest.

- In Aberdeen, patients are referred to the paediatric FH specialist in the centre that's nearest to them. It is a joint clinic that the adult lipid specialist attends with the paediatric specialist. The clinics run three times a year as part of the wider metabolic service. Western Isles also has a defined referral pathway for paediatric cases.

A paper by Professor David Wald in The New England Journal of Medicine has proposed screening for FH in children at the point of routine immunisations and for this to be a potential channel for identifying parents.[14] The logistics and cost implications of embedding this approach widely need further study but health economic modelling demonstrates it is likely to be cost effective and below the usual NICE threshold for implementation. Eventually, this method could alleviate the pressure on specialised FH services for adults if affected individuals are identified at the point of routine immunisations in the first year of life and their families are subsequently traced back.

> **"Health economic modelling demonstrates screening for FH in children is likely to be cost effective.**

It is recommended that the UK National Screening Committee (UKNSC) consider bringing child-parent screening into policy. This already has the widespread support of the national FH steering group (NHSE, PHE, HEART UK and the BHF et al.).

Engaging HCPs

Reaching HCPs in hospitals and general practice continues to be an area of disparate development. Staff awareness around FH genetic testing, referral process, ability to triage and make referrals varies significantly from one locality to another. There doesn't appear to be an optimised, agreed mechanism with which to bring HCPs on board, or for dissemination of FH service provision access and best practice evidence. One route to combat this may be to produce email bulletins

on platforms that most doctors, nurses and allied health professionals are already subscribed to, such as CCG bulletins, BMA and Royal College alerts, NICE alerts and GP Notebook.

In contrast, in some areas in Scotland engagement of HCPs has elicited inappropriate referrals from primary care, which could easily have been managed within primary care. Avoidance of these cases will require ongoing input and streamlined communications across primary and secondary care services.

> **“Models such as STPs, ICS and primary care network provide opportunities for different parts of the system to come together.**

Building networks and relationships also continues to be of importance as expected, and the role of AHSNs has been pivotal in bringing system leadership together. Models such as STPs, ICS and primary care network have provided additional opportunities for different parts of the system to come together. For instance, nursing colleagues across the North East and Yorkshire and Humber came together in autumn 2018 to focus on regional planning for cross-area referrals, and to develop insights of neighbouring area’s service models and professional peer support networks. The group was initially supported by the BHF; however, it is anticipated to be self-sufficient moving forward.

Reaching the public

Service providers continue to increase awareness of FH and genetic testing among the public. This can be particularly time-consuming and costly, which is why innovative approaches that have an extensive reach are worth exploring. One geographical area, for instance, screened a HEART UK video on FH in a local cinema before the main film and this had a positive impact on numbers reached.

Case finding

In line with the updated NICE guidelines, proactive case finding is being undertaken by most FH services surveyed. This appears to be ensuring a steady flow of referrals into services; therefore, areas that are struggling to meet demand are currently less engaged.

> **“The drive for a paperless NHS may provide an opportunity to resolve issues with systematically reviewing primary care records.**

Although there is enthusiasm to adopt the guidelines, the current infrastructure is not conducive to a systematic and comprehensive review of all primary care records to identify individuals suspected of having FH. Automating this process is also unlikely to achieve high quality results given the variable completeness of patient notes in primary care databases; some are missing family history or a record of clinical signs, others are not READ coded.

The drive for a paperless NHS and converting all patient records into electronic form may provide an opportunity to resolve this; however, that will depend solely on how patient notes are coded and categorised, if at all, and how doctors continue to fill them in. If electronic health records are developed with a standardised framework for recording and coding, then the uniformity of data will help services not only identify potential FH patients but also people at risk of heart and circulatory disease or those who may have an undiagnosed risk factor.

Contact with relatives

The debate between direct and indirect contact of relatives continues to divide the healthcare community. It is largely due to lack of clarity on information/data sharing, confidentiality and consent. It has been shown over the last few years (through anecdotal and published evidence) that the direct method, whereby FH services contact relatives directly, yields better and quicker results. This is compared to the indirect method, where the index case contacts their own family members, which is inefficient in terms of the number of relatives that come forward for testing.

From a patient perspective, there is mixed preference of one method over the other. Some patients are relieved when the responsibility to explain the test and implications of the condition rests on HCPs. The direct approach may place complex burdens on healthcare services, especially where families are not open to discussing genetic risk. There is a need for national level conversations to build a realistic and practical consensus and enable an approach that is both efficient and ethically appropriate to ensure that people receive the appropriate level of care when they need it.

Planning for service provision

Current service planning and business case proposals continue to deliver variable outcomes across the country. Some have successfully secured service provision on the basis of economic efficiency while others have integrated FH services into existing service infrastructure (for example, into lipid services) to ensure longevity.

As one service put it: "We knew the only way to make it a robust, longstanding service was to integrate within our existing service, and to work in the same way. Otherwise, we would have just lost the whole of the FH service, if you just stuck to an FH nurse who needed separate funding."

Similarly, in Scotland FH genetic services are part of existing infrastructure. Although that means better access to genetic testing, it also means that little time or resource have been invested in establishing a standardised approach to FH service provision. Services in Scotland are variable and unique to each locality, making it difficult to provide a consistently high quality of care. In some areas pharmaceutical industry involvement was cautiously accepted as a means to continue running FH clinics.

A vast proportion of services still feel that it would be beneficial to have sight of successful business cases and access to a central platform for standard operating procedures (SOPs), consent forms, shared experience of information governance approval for PASS and other standardised documents.

For instance, the Yorkshire and Humber service covers a huge geographical area spanning 18 CCGs. The development of this service was complex and took longer than other services. It was a similar case for the West Midlands service that even had to go through a Europe-wide procurement exercise for its genetic testing capabilities due to its size. There are many lessons to be learnt from sharing the process of setting up such a service, especially as the NHS is gearing up to operate at scale across regions rather than in pockets of excellence. The two case studies (see below) provide a lens on how the West Midlands and the Yorkshire and Humber services were established and developed to that effect.

Case study: Service setup and delivery at West Midlands

This region runs a primary care-based model for FH testing. It was chosen as it was felt to be more feasible for CCGs and predicted to be more cost effective. This was also in line with current priorities regarding patients' access; that is, closer to home and in the community. Set up as a hub and spoke model, it comprises the GP or lipidologist referring patients with cholesterol >9 mmol/l into FH clinics. Nurses allocate patients to a clinic nearest to their home where FH specialist nurses undertake a full assessment and the blood samples are sent to the Bristol lab. Where results are positive, patients are invited to FH clinics to discuss implications and begin the cascade screening process. Patients are referred to a lipidologist for one-off assessment and advice on medication, followed by discharge to the GP.

The ambition to roll out a West Midlands-wide FH service goes back to 2013. In 2015, the business case was developed by NHSE West Midlands, which was driven forward by one lipidologist. They worked with all 22 West Midlands CCGs to get their commitment to the programme and the entire process was led by one CCG – Birmingham Cross City, as the lead commissioner – to get all the CCGs to sign up and gain their commitment.

> **"What worked well for West Midlands was the robust business case with detailed financial modelling and having a lead commissioner from the start.**

Their contracts and finance team contacted all their counterparts across the region to get behind the business case. What worked well for West Midlands was the robust business case with detailed financial modelling and having a lead commissioner from the start. Moreover, the medical director at NHSE West Midlands wanted to standardise FH service/care across the region.

After securing the BHF funding, the lead commissioner became aware that not all CCGs were in support of the bid and associated costs, nor had all cost implications been shared with accountable officers. Subsequently, a full proposal had to be developed for CCGs to consider formally before any funding was drawn. The data sharing agreement for the PASS system also took much longer than expected and was a complex process.

Moreover, there were delays with securing a contract for genetic testing due to a need for EU-wide procurement exercise given the size of the service.

Timelines for service mobilisation were too ambitious as nurses recruited with different specialist skillsets required various forms of training given the complexity of the service and the multitude of stakeholders. Initially a phased roll-out was introduced, with subsequent aims for full coverage across the region. Sustainability of the service beyond the first four years is covered by the current business case. They are also aligning the individual specialist nurses to STP footprint areas. Their steering group is generally hosted by NHSE with the main purpose being to discuss issues, resolve clinical questions and provide updates on finance, milestones and obstacles. They also have an FH operational group and an information governance group.

Case study: Service setup and delivery at Yorkshire and Humber

This is a secondary care-based model for FH testing. This was chosen as it fits with the current model for clinical management of FH patients. FH clinics in the service are run alongside existing lipid clinics based at four main trusts: Calderdale and Huddersfield NHS Foundation Trust, Hull University Teaching Hospitals NHS Trust, Leeds Teaching Hospitals NHS Trust and York Teaching Hospital NHS Foundation Trust.

Primary care and cardiology services refer patients with suspected FH to the FH clinics for assessment; patients are evaluated for suitability of entry into the FH cascade testing pathway. If the diagnosis of FH is confirmed, cascade testing is then undertaken for affected families and an annual structured review is offered to patients with FH. Family members identified by cascade testing are referred to a lipid clinic for assessment and initial management, with an ongoing management plan agreed within primary care.

The Yorkshire & Humber region was involved in planning and developing an FH service from 2008 due to the work and enthusiasm of an HCP with a special interest in FH. In 2015, the Yorkshire and the Humber Strategic Clinical Network (Y&H SCN) supported a bid to the BHF to develop a regional FH service across the North East and West of the region. The consortium bid was based on a lead provider (York Teaching Hospitals NHS Foundation Trust) and lead commissioner (NHS Vale of York CCG) model. Funding commitment from the CCGs was secured by the relevant stakeholders in the lead provider and the lead commissioner groups, with support from the Y&H SCN. Serendipitously, there was already an existing service covering South Yorkshire, and so with the new service proposed the entire region has service provision.

When setting up the service, Yorkshire and Humber strategic leads contacted existing services about their service, model and SOPs/consent forms/ documents. The service was aligned to the nearest matching model and mirrored best practice. A steering group was established to develop the clinical pathways and a project board that ratified the clinical service model, governance and the associated financial costs.

The lead contractor and provider were not agreed on a phased approach. Agreement from most North and East Yorkshire CCGs was obtained before

starting the service to ensure clarity regarding costs and the number of nurses required. However, four CCGs were not committed to join the service. Due to the BHF's influence and the ensuing galvanisation of BHF nurses, local MP and patient representatives, three of the four CCGs have since joined.

The service would have benefitted from a phased approach, starting initially in West Yorkshire where all CCGs are committed. The service is across four hospitals and nurses are based at each hospital; the lead provider, York Teaching Hospitals NHS Foundation Trust, is the employing organisation for all the nurses. A steering group was established to develop the clinical pathways, discuss progress and logistics, and to provide feedback on key documents. Y&H SCN were part of the steering group and the project board; they handed over to the steering group in March 2016.

For both services highlighted in the case studies, it was evident that there is a need for one or two organisations to take a lead on securing commitment from CCGs (lead commissioner, lead provider). Support of the local SCN and organisations like the BHF and AHSNs is also important. A robust business case with detailed financial planning is at the core of setting up a successful service. Delays were caused in both areas due to necessity to secure commitment from a large number of CCGs and having clarity on all aspects of the service, including model, costs, and staff posts required.

There is an acute sense from services that, due to mounting pressures and stringent resources, they are set up to be primarily reactive and unable to plan and evolve. For instance, there is no resource or 'head space' to conduct any benchmarking analysis against other services or to partake in horizon scanning to identify opportunities for merging with other genetic services, or to conduct any feasibility studies on expansion. There is little room for strategic planning or to address issues that crosscut geographies. For example, the difficulty in recruiting and access to genetics training for FH nurses has been highlighted as an issue, especially in rural localities.

This begs the question as to whether there is a need for an evolution of the specialist FH nursing roles into inherited cardiac conditions (ICC) nursing roles, who can then work across a wider range of related conditions. Another possibility is for the FH nursing role to be better embedded alongside services focused on CVD prevention in primary care, ensuring a focus on the education of primary care professionals in understanding clinical guidelines and implications for diagnosis and management within primary care.

3,500

More than 3,500 people in the UK have now been diagnosed with an FH gene mutation via cascade testing.

Recommendations

There has been tremendous progress in FH genetic testing across the UK over the last ten years. Policy and clinical guideline changes have evolved in support of the required focus.

However, given competing health priorities, variation in sustainable service provision and the scale of the population affected by FH, it is important for services to adapt in order to survive.

The BHF has set out its challenge for developing better ways to prevent and detect heart and circulatory diseases. Our Turning Back the Tide report on heart and circulatory diseases is a blueprint to beat the heartbreak caused by these conditions forever.[15] It requires action from all levels of the NHS.

The following are some considerations for future action in FH services based on the findings of this report:

- As part of the NHS Long Term Plan, there is a commitment to ensure that there is greater access to genetic testing to drive early diagnosis and optimal treatment of FH- for England. The integrated NHS Genomic Medicine Service must act as an enabler and a mechanism for delivering on this commitment.

- Steps must be taken across all four nations to address the lack of cohesion on managing genetic testing data: procuring a centralised genetic testing database to ensure long-term sustainability of effective testing, dissemination and data sharing should remain a key concern. Sustainable funding for a clinical registry for FH (such as the PASS-Clinical database) in England should be a priority. A UK/nationwide database that links all four nations' databases should be explored.

- Workplace planning at national and regional levels must assess feasibility of joining up or combining FH nurse roles with others such as ICC nurses, lipid nurses, high-risk CVD nursing roles in atrial fibrillation, hypertension or other clinical leads. This is so that FH services can be incorporated into existing and wider services, entrenching them systematically and widely across the UK.

- NICE and collaborating partners should consider expanding on the NICE FH implementation guide to deliver a suite of practical tools and address emerging needs and challenges faced by the workforce at a more granular level

- Commissioners, planners and service managers must place greater emphasis on generating intelligence on how services are performing and how they benchmark against others, to support strategic decision making on delivery models and provision planning.

- Strategies must be developed to ensure equality of access to FH testing services to those from different ethnic backgrounds.

- Resource and infrastructure planning and the importance of ensuring equality of access to those from different ethnic groups must be considered when embarking upon case-finding with cascade testing. This is because it is likely to lead to an increase in referrals, especially of children, and the number of paediatric clinic sessions need to be increased.

- It is recommended that the UKNSC consider bringing child-parent screening into policy.

- Paediatric genetic testing should continue to be a priority in the NHS, with a focus on solutions rather than just de-mystifying commissioning responsibilities. Agreement must also be sought on commissioning family or young people clinics, both of which would cross commissioning boundaries.

- Clinical teams should consider publicising services on a few but impactful platforms for HCPs and the public to maximise reach in an efficient manner. For example, on CCG bulletins, Royal College and BMA bulletins, high street shop fronts and cinemas.

- Consideration should be given to convene national bodies to influence the design of standardised coding and digitising patient records. This would maximise data capture and allow for easier identification of people living with various conditions and risk factors.

- There must be national/senior-level conversations to resolve the discrepancy around the contact methods for relatives so that there is a standardised protocol for doing so, driven by the person's health needs as the foremost concern.

References

1. Henderson et al (2016) The genetics and screening of familial hypercholesterolaemia. J Biomed Sci. 2016; 23: 39 https://dx.doi.org/10.1186%2Fs12929-016-0256-1

2. Sharifi et al (2016) Cardiovascular risk stratification in familial hypercholesterolaemia Heart. 102(13): 1003–1008. https://dx.doi.org/10.1136%2Fheartjnl-2015-308845

3. BHF (2016) Delivery of familial hypercholesterolaemia services: identifying enablers and barriers https://www.bhf.org.uk/informationsupport/publications/healthcare-and-innovations/delivery-of-fh-services-identifying-enablers-and-barriers

4. NHS Genomic Medicine Service https://www.england.nhs.uk/genomics/nhs-genomic-med-service/

5. NICE (2017) Familial hypercholesterolaemia: identification and management (CG71) https://www.nice.org.uk/guidance/cg71/chapter/Recommendations

6. Haralambos et al (2015) Clinical experience of scoring criteria for Familial Hypercholesterolaemia (FH) genetic testing in Wales. Atherosclerosis. 2015 May;240(1):190-6 https://doi.org/10.1016/j.atherosclerosis.2015.03.003

7. Heart UK (2014) Systematically identifying familial hypercholesterolaemia in primary care: an audit within the Medway Clinical Commissioning Group. https://medwayccg.nhs.uk/component/rsfiles/download-file/files?path=about%252FAnnual-Report%252FFH.pdf&Itemid=414

8. Weng et al (2015) Improving identification of familial hypercholesterolaemia in primary care: derivation and validation of the familial hypercholesterolaemia case ascertainment tool (FAMCAT). Atherosclerosis. 2015 Feb;238(2):336-43 https://doi.org/10.1016/j.atherosclerosis.2014.12.034

9. PRIMIS/University of Nottingham (2018) CVDprevent: a national primary care audit – feasibility report. https://www.bhf.org.uk/for-professionals/healthcare-professionals/innovation-in-care/cvdprevent

10. Public Health England/NICE/NHS England/NHS RightCare/BHF/HEART UK (2018) Familial hypercholesterolaemia: Implementing a systems approach to detection and management https://www.gov.uk/government/publications/familial-hypercholesterolaemia-implementation-guide

11. NHS England (2016) Improving Outcomes through Personalised Medicine https://www.england.nhs.uk/publication/improving-outcomes-through-personalised-medicine

12. NHS England (2019) NHS Long Term Plan https://www.longtermplan.nhs.uk/

13. Data from PASS database, presented by the National PASS Data Co-ordinator and Professor Steve Humphries

14. Wald et al. (2016) Child-parent familial hypercholesterolemia in primary care. N Engl J Med. 2016;375:1628-1637 https://doi.org/10.1056/NEJMoa1602777

15. BHF (2018) Turning back the tide on heart and circulatory diseases. https://www.bhf.org.uk/what-we-do/influencing-change/turning-back-the-tide

bhf.org.uk

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