Saving Scottish Lives, Saving Scotland’s Money

Report on the advantages of implementing cascade screening for Familial Hypercholesterolaemia in Scotland

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About HEART UK

HEART UK - The Cholesterol Charity - is passionate about preventing premature deaths caused by cardiovascular disease (CVD). The charity aims to help families with a high risk of premature CVD, especially those with inherited high cholesterol (familial hypercholesterolaemia, FH). More than three-quarters of people with FH are undiagnosed, (probably) untreated and thus remain at serious risk of premature death from CVD.¹ ²

About Familial Hypercholesterolaemia

FH is a relatively common genetic disorder. The estimated prevalence of FH is 1 in 500, suggesting 120,000 affected individuals in Britain (with at least 10,000 in Scotland). The condition is massively under diagnosed, with only 15,000 cases identified in the UK. Children of an individual with FH have a 50 per cent chance of inheriting the condition. Left untreated, FH may lead to premature death from CVD. 50% of males and 30% of females with untreated FH will develop coronary heart disease before the age of 55.³

FH in Scotland

Scotland’s Better Heart Disease and Stroke Care Action Plan (2009) includes the following actions on FH:

- “A national forum for FH should be established by SGHD [Scottish Government Health Directorates] to raise awareness of FH among primary care professionals, to prioritise the need for diagnosis, to define and agree referral protocols, and to develop good practice for clinical investigations, genetic testing and cascade screening within families” (para 4.97)
- “The Aberdeen molecular genetics laboratory should develop a funding proposal for a pilot project of cascade testing for FH, for submission to CSO [Chief Scientist Office]” (para 4.100)
- “The NCDDP [National Clinical Datasets Development Programme] should be extended to include familial hypercholesterolaemia” (para 7.8)⁴

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Foreword

These days it is very common to see the phrase ‘prevention is better than cure’ in much of health policy. However, the application of the principle is not nearly so common. Familial hypercholesterolaemia (FH) is a case in point. FH is a relatively common genetic condition, affecting some 10,400 Scots. When FH is undiagnosed and untreated, whole families may suffer long-term morbidity and premature mortality from heart disease. If untreated, the risk of developing cardiovascular disease is an incredible 84 times more likely than for the general population aged less than 40 years. Yet with effective, affordable means of diagnosing and treating FH readily available, we have an opportunity to stop these early deaths now.

In Scotland, inroads have been made in recent years towards improving the diagnosis and treatment of those with FH. Some 2,000 people have been genetically tested for FH, with almost a quarter of those tested so far definitively diagnosed with the condition. Yet this means there is still a long way to go to find the remaining people with FH. A national programme for Scotland is needed - one that better identifies possible cases of FH in primary care and coronary care units; establishes a joined-up system for registering patients and testing their relatives; and provides improved access to secondary care lipid clinics where required.

If 50% of FH were to be identified and treated, NHS Scotland could save approximately £149,000 per year, largely because expensive cardiovascular procedures and emergency treatments would be avoided. The long term impact of the failure to identify and treat FH will have a significant effect on the economy in terms of loss of employment potential and dependency of welfare payments.

In this report, HEART UK has examined the evidence in three critical domains – health economic modelling, the research literature, and, perhaps most importantly, through interviews with patients and clinicians. We hope that NHS Scotland will consider the recommendations put forward in this report, and would welcome the opportunity to be involved in their further development and implementation.

Jules Payne
Chief Executive, HEART UK
Executive Summary and Recommendations

In Scotland it is estimated that there are approximately 10,400 people affected by FH. If 50% of FH cases were to be identified and treated, NHS Scotland could save approximately £149,000 per year. Left untreated, people with FH are at considerable risk of developing premature CVD. The long term, iterative impact of the failure to have identified and treated FH in the past will be having a significant effect on the economy in terms of loss of employment and dependency of welfare payments. Yet we can reduce this burden in the future. Identifying and treating people with FH, coupled with effective cascade screening, has the potential to save NHS significant resources and improve the quality of life for a large number of people and their families.

Research has demonstrated that with the advent of statins to modify disease progression, there is an increased emphasis on the early diagnosis of affected individuals and their relatives. Whilst there are debates about the cost and clinical effectiveness of different methods of testing, there has, until recently, been less written about the patient experience of genetic testing and cascade screening.

This report highlights the economic benefits of cascade screening and early detection of FH, reviews current research and reports on a series of one-to-one interviews with clinicians and Scottish patients with FH.

In concluding this work, HEART UK makes the following recommendations.

1. **Additional specialist lipid clinics**

NHS Scotland should address the under provision of lipid clinics to ensure parity for patients across Scotland. Specialist lipid clinics are critical for the assessment and treatment of people with FH and other complicated lipid disorders. A recent paper on cascade testing for FH recommends that a lipid clinic is needed for every 200,000 people. At present, Scotland is sorely lacking in lipid clinics, as illustrated in Appendix 2. There are none in Fife, Lanakshire, Borders, Dumfries and Galloway or any of the island health board areas and patients in Highland, Grampian and Tayside have to travel significant distances to access the ones in Inverness, Aberdeen and Dundee.

2. **Development of FH family-based patient registry and follow-up system**

For this report, discussions took place with clinicians and patients alike. In most cases, FH patients were referred to specialist lipid clinics as a result of an especially high cholesterol being detected initially in primary care. It was rare for patients to be

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referred for secondary care treatment as a result of high cholesterol being found in other family members. This suggests that, although people with FH are slowly being found in Scotland, they are mostly index cases, indicating that cascading through other family members is not happening as often as it should. NHS Scotland should consider investment in systems to ensure a consistent and cohesive approach to identifying and screening FH patients across Scotland.

A specific database application for FH which includes registry, advanced pedigree drawing of family trees, workflow management and reporting functions has been developed by PASS Software and has been successfully implemented in the national FH cascade screening programme in The Netherlands. PASS Software has now been adapted for use in Wales and is currently being further modified for England. In previous publications, HEART UK has demonstrated that PASS software provides an efficient and low-cost system for cascade testing, linking clinicians, and registering patients.

HEART UK believes that using PASS software will be beneficial for all parties. Patients will benefit as more cases are being referred, documented and treated. For minimal cost, NHS Scotland will establish an FH patient registry and software that enables cascade screening. NHS Scotland will also gain a useful reporting mechanism which is part of the system. A variety of reports can be created which, for example, can produce information about number of index patients, number of second and third degree relatives, types and quantities of genetic mutations, and a host of patient categories and vital statistics. Finally, the clinical community will benefit, as they will be better connected and equipped to carry out cascade screening for FH.

3. Family history taken in coronary care units

People under 50 who appear in coronary care units should have their family history discussed as routine, with consideration of the possibility of FH and referral process undertaken as necessary. Furthermore, instances of death from heart disease under the age of 50 could be considered for genetic testing, with appropriate cascade testing if necessary.

4. Identification of elevated cholesterol at primary care health checks

This report found that patients and clinicians alike felt that greater public awareness of FH is needed to help in the primary prevention of CVD. Primary care would be a valuable route to help increase awareness and detection of the condition. Opportunities to find possible cases of FH through screening should therefore be considered.

6 http://medic.cardiff.ac.uk/archive_subsites/ / _/medic/subsites/fhproject/index.html

7 See HEART UK (2012) Saving lives, saving families: The health, social and economic advantages of detecting and treating familial hypercholesterolaemia.
Scotland’s Keep Well health check programme may be one such route and in line with the Health Check programme in England, people identified as having cholesterol above 7.5 mmol/L and a family history of early heart disease should be considered as possible cases of FH (with recommended clinical processes then followed before confirmation). A very highly elevated cholesterol may indicate FH, so it would be important to follow up with a family history to ascertain whether the individual would be classed as “probable” FH, in accordance with the diagnostic tool known as the Simon Broome criteria.8

5. Appropriately trained staff to conduct cascade testing

To conduct proper cascade testing, Scotland needs to employ more healthcare professionals (HCPs) with expertise in genetics, family counselling and dietetics. These HCPs could be a nurse with specialist training in family care, paediatrics, dietetics and pharmacy. The research literature demonstrates the complicated nature of familial conditions. HCPs treating patients with FH should be given sufficient time and opportunity to explain results and listen to patient concerns and queries.

Chapter 1

Economic Report on Familial Hypercholesterolaemia (FH) Screening in Scotland

The purpose of this chapter is to provide an overview of the economic impact of cascade screening for the FH population in Scotland. The following report is intended as an addendum to the recent HEART UK publication, Saving Lives, Saving Families,9 10 which pertained to England, while this document focuses on the Scottish data available. Both reports draw from the NICE Guidelines on FH - for example, when considering levels of FH in the population and treatment options. Links to the Guidelines are provided in the footnotes.

In Saving lives, saving families, a cost-utility analysis was conducted to quantify the benefits of optimal, high intensity statin treatment or sub-optimal statin treatment compared to no treatment. Lifetime treatment costs and health benefits were calculated in line with NICE guidance. The analysis showed the benefits of treatment in terms of QALY (quality adjusted life year) gains and cardiovascular (CV) events avoided. The study also showed the benefits of cascade screening and associated savings from various levels of implementation. More effective treatments will reduce the incidence of CV events and in the long run save money to the NHS, compared with less effective interventions.

In that analysis, as in this report, cases were considered over a 55 year period; from the age of 30 until 85 years, with costs and QALYs calculated until patients either died or reached the age of 85. The benefits of diagnosing and treating people with FH are cumulative over time, as more CV events are avoided. The result is that the more people being treated, the greater the benefits to individuals and the public purse. The English findings are also reflective in this report for Scotland.

9 HEART UK (2012) Saving lives, saving families: The health, social and economic advantages of detecting and treating familial hypercholesterolaemia
Background and Context

Familial Hypercholesterolaemia (FH) is a relatively common condition affecting 1 in 500 people. If left untreated, people with FH suffer a much higher premature death rate from cardiovascular disease than the general population. If untreated, approximately 50% of men and 30% of women with FH will develop coronary heart disease, (CHD) by age 55. Detection and treatment are inexpensive and straightforward, and reduce the risk for FH.\textsuperscript{11}

The National Institute for Clinical Excellence, (NICE) has published a guideline recommending that those at risk of FH should be identified by cascade testing, (where immediate and then more distant relatives of people with FH are screened for the disease).\textsuperscript{12} This guideline shows that this combination of cholesterol and DNA testing in families, followed by lipid-lowering therapy, is clinically and cost effective. NICE have also estimated that this would result in quality adjusted life year (QALY) of £2,700, which is well below the threshold of approximately £20-30,000 per QALY. Further economic analyses commissioned by HEART UK has shown that in the long run, effective screening and treatment will lead to savings for the NHS; the higher the number of people screened, the lower the cost of each screening. The Scottish Intercollegiate Guideline Network (SIGN) has also published a guideline on screening in Scotland.\textsuperscript{13}

Scottish Population Data

NHS & Health stats:

- The estimated prevalence of FH in the UK is 1 in 500. This means that there are approximately 10,400 affected people in Scotland, based on the Scottish population of 5.2 million.\textsuperscript{14}

- If untreated, the risk of cardiovascular disease in this group of patients is about 84 times more likely than the general population for those aged less than 40 years, compared to an increased risk of 20% for those aged over 60 years.\textsuperscript{15}

- In the 2011 Scottish Government heart disease statistics report, it was stated that despite the continual downward trend in rates of cardiovascular mortality over the past 10 years, rates of decline of mortality for men and women aged 35

\textsuperscript{11} Ibid \textsuperscript{12} National Institute for Health and Clinical Excellence (2008) Quick reference guide for NICE clinical guidelines; 71 \textsuperscript{13} http://www.sign.ac.uk/pdf/sign97.pdf \textsuperscript{14} http://www.scotland.org/facts/population \textsuperscript{15} National Institute for Health and Clinical Excellence (2011) Review of clinical guidelines (CG71)- Identification and management of family hypercholesterolaemia. Appendix E economic costs
to 54 years have flattened out and that a significant proportion of these individuals could have FH.\(^{16}\)

- Using optimal lipid-lowering treatments compared to no treatment has been shown to avoid 101 deaths per 1,000 FH patients treated, as lifetime events avoided in patients followed up between 30 years and 85 years\(^{17}\). This means 1,000 deaths avoided in Scotland alone, based on numbers of people with FH.

- If 100% of FH cases are identified and treated optimally over a 55 year period, Scotland could save \(\mathbf{\text{£30.2M}}\), or \(\mathbf{\text{£596,667}}\) in health costs per year\(^{18}\)\(^{19}\).

- If, more realistically, 50% of FH cases are identified and treated, Scotland could save in health costs over 55 years \(\mathbf{\text{£8.2M}}\), or \(\mathbf{\text{£149,000}}\) per year. The benefits of treatment are cumulative, meaning that the higher the numbers treated the fewer costs for CV events that would have otherwise occurred.\(^{20}\)

- By not fully implementing the cascade screening as recommended in the NICE guidelines (that is, identifying 50% of potential cases), the NHS in Scotland could be losing approximately \(\mathbf{\text{£100,000}}\) per year.\(^{21}\)

**Non-NHS & Health stats:**

- These savings do not include other wider savings external to the NHS, such as costs of disability and sickness benefits, social care costs and costs to the economy because of tax-paying years lost, as well as the social costs to families and the community.

- In 2006, production loss due to mortality and morbidity associated with cardiovascular disease (CVD) cost the UK over \(\mathbf{\text{£8.2 billion}}\), with around 55% of this cost due to death and 45% due to illness in those of working age.\(^{22}\) Using

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16 \[http://www.scotland.gov.uk/Publications/2009/06/29102453/6\]
17 HEART UK (2012) Saving lives, saving families: The health, social and economic advantages of detecting and treating familial hypercholesterolaemia
18 Management of Coronary Heart Disease; A National and clinical impact assessment 2007; SIGN
19 See analysis at HEART UK (2012) Saving lives, saving families: The health, social and economic advantages of detecting and treating familial hypercholesterolaemia
20 Ibid.
21 Ibid.
proportionate analyses for Scotland, this means that the cost of CVD (but not FH specifically) to Scotland due to production losses was £738M in 2006.

- Overall, CVD is estimated to cost the UK economy nearly £9.0 billion a year, of which around 47% is due to direct healthcare costs, 27% to productivity losses and 26% to the informal care of people with CVD.\(^{23}\) This means that the total cost, including health care, loss of productivity and the informal care of people with CVD is approximately £810M in Scotland.

- Given the younger age profile of those with FH, it is probable that the loss to the economy in terms of productivity and informal care will be proportionately higher.

- After NICE published its guideline, representatives of the Scottish Lipid Forum met to discuss the potential implications for Scotland. Genetic services had been available in Aberdeen prior to this, but it had been underused. Some Health Board areas such as Highland, Lanarkshire and Fife had no lipid clinic provision at all.

- In 2010, a process of cascade testing was introduced and according to the Scottish Lipid Forum, by 2013 2,000 people had been tested and 400 people found with FH. This means that there is still a lot of progress to be made to find the undiagnosed FH population.

**Conclusion**

The evidence reviewed above supports the case for a more coherent and consistent approach to cascade testing, as well as for the effective treatment of FH by use of lipid-lowering therapy.

If 50% of FH patients were to be identified and treated, NHS Scotland could save approximately £149,000 per year or £8.2million over a 55 year period – that is, if treatment commences at the age of 30 and continues until the age of 85. Left untreated, people with FH are at considerable risk of developing premature CVD. The long term, iterative impact of the failure to identify and treat FH will have a significant effect on the economy in terms of loss of employment potential and dependency of welfare payments.

Identifying and treating people with FH, coupled with effective cascade screening, has the potential to save the NHS significant resources and improve the quality of life for a large number of people and their families.

\(^{23}\) Ibid
Chapter 2

Familial Hypercholesterolaemia: Understanding the Patient Experience - A Review of Existing Research Literature

Familial hypercholesterolaemia (FH) is a relatively common inherited autosomal dominant disorder characterised by high concentrations of low-density LDL cholesterol in the blood, which in turn makes those affected more likely to suffer premature CHD and death.

The majority of people with FH have inherited a single mutation from one parent in either the LDL receptor (LDLR), apolipoprotein B (APOB), or proprotein convertase/kexin type 9 (PCSK9) genes. The majority of those with FH remain undiagnosed, untreated or inadequately treated. 24 The criteria for a clinical diagnosis of FH include a high LDL-C concentration in adults plus a family history of raised cholesterol or early CHD in a first degree relative. 25

The purpose of this chapter is to explore the extent to which existing literature on FH examines the patient experience of genetic screening. Our focus was on literature based qualitative studies of patients and their response to cascade screening. We also reviewed more generic literature relating to chronic conditions with a familial cause.

There has been an increased emphasis on the importance of understanding and improving the patient experience of health care in Scotland, exemplified by Better Health, Better Care (2007). In addition to delivering effective and safe care, NHS Scotland is committed to delivering care that is patient centred. At the same time, we have witnessed an increased use of genetic testing and screening to assess a patient's risk of developing or inheriting specific illness. Whilst genetic testing and screening inform health choices and enable healthcare professionals to provide targeted treatment, the patient experience of this process also needs to be explored.

What follows examines the different meanings attached to and experiences of genetic testing and cascade screening for healthcare professionals and for their patients.

Genetic testing and cascade screening: a clinical process

Much of the existing literature focuses on the testing and screening as a clinical process. Wald et al (2007) 26 looked at methods for developing a population screening strategy

for FH to prevent elevated mortality from CHD. Cascade screening of first degree relatives of affected individuals is one possible option. However, the authors argue there is no effective way of identifying index cases in the population, so uncertainty remains over the what screening strategy is likely to be most effective.

Based on a meta-analysis of published studies in total LDL cholesterol, in individuals with and without FH, to determine at what age cholesterol measures discriminate best between those affected and those not affected, the authors propose that the most effective screening is by measurements of serum cholesterol done in early childhood after the first year of life.

Wald et al argue that for every affected child there would be one affected parent, identifiable as the one with the higher serum cholesterol concentration. They conclude that such a proposed child-parent screening strategy has the potential to prevent the medical consequences of this disorder in two generations simultaneously.

The paper does not consider the patient experience other than in the context that blood sampling could take place at the same time as routine childhood immunisations

“...when parents are receptive to the possibility of preventing disease in their child and therefore may be receptive to a family based strategy to prevent the consequences of the same disease within the family as a whole.”

Other papers have concentrated on reviewing the effectiveness and cost effectiveness of using alternative diagnostic and screening strategies. Nherera et al (2011) set about estimating the probable cost-effectiveness of cascade screening methods in FH. The authors conclude that cascade screening from index patients with both clinically defined definite and possible FH is highly cost-effective when using a combination of DNA testing for the family mutation when it can be found and LDL-cholesterol levels when it cannot. They also conclude that cascade screening to identify relatives of patients with FH is also more cost-effective than recently recommended primary prevention screening strategies.

Izar et al (2010) provide us with an overview of current screening methods for homozygous and heterozygous FH. Interestingly, Izar and colleagues’ paper also considers the ethical implications of genetic screening; firstly in relation to accessing health insurance and, secondly, in relation to a right to privacy.

Leren (2004) argued that the most cost-effective strategy to diagnose patients with FH is to screen close relatives of patients already diagnosed with FH; that is to carry out cascade screening. The authors reviewed the organisation of a cascade genetic screening program for FH as well as cost-efficiency assessments, health benefits,

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possible adverse effects, and the screening of children. The author concludes that cascade genetic screening for FH leads to health benefits and is cost-effective without causing psychological or social damage. Accordingly, national cascade genetic screening programs for FH should be part of ordinary health care.

**Genetic testing and cascade screening: the patient journey**

With the advent of statins to modify disease progression, there is an increased emphasis on the early diagnosis of affected individuals and their relatives. Whilst there are debates about the cost and clinical effectiveness of different methods of testing, there has, until recently, been less written about the patient experience of genetic testing and cascade screening.

Hallowell et al (2011) examined the experiences of DNA cascade screening of 38 patients in the Lothian region of Scotland. The majority of research participants had a positive experience of DNA testing and found that drawing up a detailed pedigree helped explain their family's risks in relation to FH. This in turn paved the way for a discussion with family members about who needed to be informed about their risk and who needed to be screened.

Hallowell et al argue that DNA testing does help facilitate insight into the genetic transmission of FH and, thus, provides the means to initiate communication with relatives. The authors acknowledge that the index patient in these instances may be more willing to communicate with relatives because the condition can be treated effectively and is not stigmatising, compared to other conditions.

The authors of the Lothian study also offer guidance on the most effective methods of accessing relatives for cascade screening. Existing research supports the idea that direct contact by a member of the clinical team increases the number of family members coming forward for cascade screening. However, such an approach does raise ethical issues about privacy and data access.

Patients who had undergone DNA testing expressed a preference for taking the initial responsibility for contacting ‘at risk’ relatives, rather than having clinical staff approach them unsolicited. This paper suggests, therefore, that indirect methods for cascade screening can be beneficial, but the advantages of such an approach must be weighed against the potential for reduce uptake of screening. The authors conclude that additional research is needed to compare index patients’ and family members’ experiences of different methods of cascade screening.

Hallowell et al also point out that this area requires additional research to compare index patients’ and family members experiences of the different methods of familial cascading used in this study.

Hollands et al (2012)\textsuperscript{30} offer insight into patient experience of diagnostic testing for FH, comparing responses to genetic and non-genetic testing methods. Based on a series of interviews with 39 patients, this paper concluded that the impact of diagnostic testing did not seem to vary on the basis of whether or not genetic information was used. Overall, the authors suggest that being given a formal diagnosis of FH appeared to have minimal impact of the lives of those who participated in the research.

The lack of impact may be in part be explained by the fact that most patients had a realistic expectation that their diagnosis would be positive, thus confirming their beliefs and their experience of having relatives with either FH or high cholesterol. The patients reported that a positive diagnosis actually helped reduce their uncertainty about their health. For those who tested positive, the diagnosis can be the means to explain their high cholesterol to others in terms of FH being hereditary, rather than as a consequence of unhealthy life choices on their part.

Hilgart et al (2012)\textsuperscript{31} examined the patient experience of being tested ‘negative’ for FH. This research, based on 11 patient interviews, explores three inter-related themes: ‘feeling in limbo’, ‘exploring the causes of raised cholesterol’ and ‘contradictions in talk about diet’.

For those individuals with a clinical diagnosis of FH but for whom no genetic mutation has been found, the challenge is to explain and understand their condition. This state of uncertainty is in contrast to those given a positive diagnosis who, as Hollands et al indicate, may well find the diagnosis reassuring.

Hilgart et al found that participants were actually anxious to confirm the cause of the hereditary problems they had witnessed in their families and, sometimes, in themselves as well. A negative test result left patients uncertain as to the cause of their raised cholesterol. Some patients interpreted the results to mean that they did not have a hereditary condition but others challenged the results in as far as they did not take the results for granted; one participant remained convinced that she has a ‘rarer form of FH’.

Patients with a positive diagnosis of FH appear to have a clear pathway to follow, as indicated in the work of Hallowell et al; patients are, for example, provided with information to pass on to relatives and relatives are encouraged to participate in cascade screening. However, no such clear pathway emerges for patients with a negative diagnosis. Hilgart et al suggest that patients do not have clear expectations about their own health, their children’s health and their future healthcare eligibility in relation to FH.

\textsuperscript{31} Hilgart et al 2012 Individuals experiences of, and responses to, a negative genetic test result for familial hypercholesterolaemia - J Health Psychol. 2013 Mar;18(3):339-49
Although Hilgart et al’s work is based on small numbers, it does raise interesting issues about how health care professionals deal with patients with negative diagnosis of FH. The author suggests that we need to reflect on how the results of genetic testing are communicated. The participants in this study, for example, would have welcomed the opportunity to talk through their results with a health care professional from the lipid clinic to clarify what the test implied for their future care.

Just as confirmation of FH seems to provide comfort to those who test positive, a negative test result leads to a state on confusion and uncertainty. For many, there was a strong sense that a genetic reason was the only plausible explanation, given that most claimed to lead a relatively healthy life. Participants were left with seeking a more complex, multi-factorial explanation, including environmental and lifestyle factors.

Other studies have focused on the ways in which patients perceive their vulnerability to FH as a means to explore how clinicians may communicate more effectively with their patients. Frich et al (2006)\textsuperscript{32} undertook a qualitative study of 40 patients with FH. The authors found that patients negotiated a personal and dynamic sense of vulnerability to CHD that was grounded in their personal perceptions of genetic and inherited risk. When patients were calculating their personal risk of CHD, they did so by consulting their family history, focusing on age, lifestyle, cardiac events and cardiac deaths. The study concluded that participants attributed most importance to first and second degree relatives they knew, or thought, had FH.

When the patients in the study assessed their personal vulnerability to CHD, they did so by assessing and comparing their lifestyle with that of the relatives with, or assumed to have, FH. Patients felt that living a healthy lifestyle, exercising and taking lipid-lowering medicine made them less vulnerable than their relatives.

Frich et al (2006) conclude that knowing how patients calculate their personal risk will help clinicians communicate more effectively. Research suggests, for example, that patients are more motivated to seek medical treatment if they are provided with personally relevant information rather than information about ‘average’ risk. It is recommended, therefore, that clinicians assess each patient’s risk of CHD individually, based of information gleaned from a family history.

The onus is on clinicians to listen carefully to a detailed family history in order to gain a clear understanding of the patient’s perspective. The authors suggest that the point of this dialogue is to clarify potential misunderstandings and provide a common ground for a shared understanding and decision making.

There is a growing body of literature looking more generally at lay understanding of familial risk of chronic diseases and this research can add to our understanding of the

patient experience of FH. Walter et al (2004)\textsuperscript{33} undertook a systematic review of literature in this area to reveal that there are some similarities and some significant differences in the ways in which lay people and health care professional assess risk. Some features of lay beliefs mirror medical tools used to assess risk; one example being the number of affected relatives. Other features of lay risk assessment are more individual and personal; examples include experience of a relative’s disease, their sudden or premature death and comparisons between the patient’s lifestyle and that of relatives.

Walter et al also suggest that patients assess not only the number of family members affected, but that they make a personal comparison between themselves and the affected relatives in terms of physical characteristics, personality and behaviour. The authors also indicate the use of ‘non-medical’ criteria to assess risk and vulnerability. Additional factors, such as emotional closeness and first-hand experience of the relative’s disease also influence patients’ assessment of risk. Walter et al argue that there is a potential mismatch between the way lay and professional groups understand familial disease, observing that: “People may wish only to manage their personal disease risk and understand the risk to future generations rather than to understand the underlying scientific explanation.”

Walter et al (2005)\textsuperscript{34} explored these themes further in their own qualitative study of family history of common chronic diseases based on 30 face-to-face interviews with general practice patients. This study confirms the suggestion that a patient’s experience of familial disease is based very much on a personal sense of vulnerability to the illness.

Whilst lay people, like healthcare professionals, counted the number of affected relatives, they also looked at a range of other factors; these included emotional closeness and personal likeness to the relative as well as different beliefs about the contribution of nature and nurture to the disease.

The authors conclude that eliciting the patient’s perspective when discussing risk in relation to chronic disease, especially in relation to family history, could inform a more patient-centred approach to risk assessment and communication and support to patients to make informed decisions about the management of their disease.


Summary and conclusion

This chapter has provided a review of the existing literature on genetic testing and screening for FH. There is disparity between those articles that see testing and screening as a purely clinical process and those that try to understand the patient experience of that process. Debates about the efficacy and efficiency of different methods of testing and screening raise valuable issues. However, they often neglect the patient story behind the process.

There is a growing body of work looking at the patient experience of testing for FH, as well as for other hereditary chronic conditions. This body of research informs us that testing is largely welcomed by patients because it provides them with a degree of certainty about their condition. The lack of fear and anxiety around testing for FH is in part because, unlike many other hereditary conditions, FH responds to treatment and the condition itself is non-stigmatising.

There is a rich vein of literature focusing on the patient understanding of hereditary risk which suggests two things; firstly, that patients perceptions mirror those of clinicians in terms of counting the number of affected relatives. Secondly, patient and clinician perceptions diverge when it comes to assessing vulnerability. Patients are likely to invoke a range of non-clinical factors when assessing their personal susceptibility to hereditary conditions; such factors including how emotionally close the person is to the affected relative and the extent to which they have first-hand experience of that relative coping with the disease.

Despite having first and second degree relatives with a hereditary condition, many patients still not consider themselves “at risk” and it may be that the inclusion of what could appear to be ‘irrelevant’ criteria in assessment of vulnerability may help explain this.

Clinicians can use these accounts of the patient experience to provide better care and support for people affected by FH. A number of the articles reviewed here emphasise the importance of listening to the patient history to identify affected relatives, but also to 'hear' the patients personal assessment of their own risk. As the previous discussion has highlighted, there is a danger that the patient might be able to ‘explain away’ their risk by referring to important but non-clinical criteria; for example, that they are physically different to their affected relatives and have a healthier lifestyle.

The receipt of a negative test result, despite having high cholesterol, is a relatively under explored area in the existing literature. Being given a negative result appears to leave patients in a state of limbo which contrasts with the certainty delivered by a positive test. Under these circumstances it appears that patients might appreciate the chance to talk through their results with staff from the lipid clinic and be given some direction about their future care pathway.
Chapter 3

Familial Hypercholesterolaemia: Understanding the Patient Experience – Interviews with Clinicians and Patients

Introduction

The purpose of this chapter is to consider and report the findings from the interviews with FH patients and clinicians working in lipid clinics in Scotland.

The aim of these interviews was to gain first-hand accounts of those affected and those responsible for the care of such patients, to establish the extent of their personal experiences and to relate this to the accounts offered in the various research documents reviewed in the previous chapter.

Methodology

For this aspect of the project, we spoke to ten patients and four clinicians involved in the running of lipid clinics. The clinicians who participated were contacted by HEART UK and followed up by a researcher at Baccus Consulting, who provided them with details of the study and the nature of their required input. Patient participants were provided with Baccus Consulting contact details by clinicians, following which ten offered to participate. Upon contact, the nature and scope of the study was outlined to the patient participant and they were fully informed of the process and the intended end result prior to their informed consent. Patients were also informed that they were at liberty to refuse to answer any question(s) they did not feel comfortable with and that they could discontinue their involvement at any time. For the purposes of this project, all comments, quotes and inputs have been anonymised and their identities remain confidential. All contact details and records kept have, in accordance with the Data Protection Act, been destroyed upon completion of the study.

Each participant was interviewed by telephone using the questions included in Appendix 1. In addition to the pre-agreed questions, all participants, patients and clinicians were provided with the opportunity to offer any additional comments, observations or inputs they felt had not been covered, but were in their opinion relevant and valid.

Clinicians

The four clinicians who were interviewed were responsible for five lipid clinics across a wide geographic area of Scotland. All defined their job titles, professional roles as chemical pathologists/clinical biochemists and all were responsible for local lipid clinics. All ran weekly clinics, with each seeing on average 15-16 patients per clinic.
The following section provides an aggregated account of their responses to the interview questions and due to the small number of participants; it has not been possible to identify geographic locations, without compromising the anonymity of the participant.

**Referral route**

All clinical participants reported that the single most common route for referral was via primary care, with most patients having been picked up during routine testing, either by means of NHS health checks such as Keep Well and/or Equally Well or, in some cases, as a consequence of work-related health checks.

**Family History**

All stated that it was rare for patients to be referred due to the detection of high cholesterol in other family members and that where there were known incidences of CHD in other family members, it was unusual for patients to have connected that with their circumstances. In other words, even where direct family member, parent and/or siblings had suffered and/or died from CHD, the majority of referred patients did not necessarily relate that to the detection of their high cholesterol.

Whilst some patients may have self-referred to GPs, this would appear to have been the exception rather then the rule and the majority of those referred to lipid clinics had had no previous concerns about their cholesterol levels and heart health.

**Genetic Testing**

All clinics covered used the commonly employed Simon Broome criteria as a diagnostic tool. Based on these criteria, those referred patients who met the conditions for FH were then offered genetic screening. In some cases the initial stages were carried out in the lipid clinic by the clinician participating, in other cases the patients were referred to the genetics service prior to any further intervention. There did not appear to be any clinical basis for this process and would seem to be an evolutionary development.

Irrespective of the point of referral to the genetics service, all clinicians reported that only if the genetic screening tested positive was any form of counselling provided. None reported any form of pre-testing counselling being provided, other than the advice and support offered by clinicians and associated staff in the lipid clinics. Many stated that this put significant pressure on their clinic time and resources with allotted appointment times gradually increasing to accommodate the additional time required to adequately prepare and support patients for genetic testing.

All clinicians reported that those patients who tested positive went on to receive appropriate and welcomed counselling. However, there was some concern expressed that this counselling was only made available to those patients who tested positive for genetic diagnosis and that the counselling was provided after the results were made
available. Clinicians felt that those who did not test positive, but yet met the diagnostic criteria using the Simon Broome register, were as much in need of appropriate counselling to help them deal with the next steps of living with their condition. It was also felt that such support could assist them in terms of dealing with the consequence of feedback to other family members, an element of the process which some considered to be more difficult without a positive test result.

There was also concern expressed regarding the potential attrition from the clinical process of those patients who have a strong family history of CHD and/or high cholesterol levels, who meet all the criteria and clinically fit the diagnosis of FH, yet who test negative at genetic testing. It was reported that as many as 50% of those who test negative are lost to the system and that clinical follow up is greatly compromised in such cases.

This raises questions about the detection of direct family members in such cases. Clinicians reported providing assistance and in some cases, “to whom it may concern” letters for those patients testing negative to assist them in communicating to family members of their risk and the benefits of seeking clinical advice. However, it was universally reported that this was by no means a desirable means of clinical follow-up. In addition to the 50% attrition rate of those “negative “cases referred to the lipid clinics, there was the added loss to the system of their direct family members who may also be at risk.

In short, whilst the advent of genetic testing and the subsequent cascade screening has been welcomed by those clinicians who participated, there was a perception of a “two tier” service with those testing positive receiving genetic counselling post test results and in addition, the process of the cascade screening enabled the patient to gain some welcome distance from the follow-up process with direct relatives. This was in contrast to the circumstances of those testing negative, yet meeting all the diagnostic criteria who received no counselling and were most often the person faced with communicating any potential information regarding risk and follow-up to direct family members. Clinicians raised concerns regarding the high level of attrition in this group of patients.

*Summary of interviews with clinicians*

- Weekly lipids clinics of approximately 15/16 patients per clinic
- Referrals almost exclusively via primary care
- Most referrals resulting from some sort of health check
- Limited number of patients referred from secondary care
- Most cases referred previously not concerned about cholesterol levels and/or heart health, even where there was previous family history of CHD, including deaths in the family
- Counselling only provided upon testing positive at genetic testing stage
- No counselling, support provided for those patients meeting criteria, but testing negative
- High attrition rate – 50% in those testing negative from the clinical system
- Concern regarding follow up of those patients and no systematic capture of direct family members
- Some concern was expressed regarding the very limited numbers of referrals from the secondary care sector, in particular those young post-cardiac episode patients and if there was any subsequent cascade screening offered.

And finally....

Clinicians participating were asked to comment on what they would like to see change, improve, and be done differently. All commented that they were finding it increasingly difficult to provide a fully-supported service within the limits of time allocated for appointments. This was a particular issue in respect of “counselling” patients prior to the genetic testing process, but more significantly in terms of the time needed to support those patients testing negative and to give them space to explore next steps and rehearse conversations with direct family members.

As stated previously, participating clinicians did provide various forms of communication/information to assist patients with this, but this was out with the scope of the expectation of the service and will clearly have resource implications. It was largely felt that there needs to be more thought and time given to the follow-up and ongoing management of those patients testing negative and their direct family members. As one clinician said, “just because the genetic test is not positive, does not mean they don’t have FH, and that they and their family are not at risk”.

All clinicians were at pains to point out that the consequences of FH are preventable and that there is a need for increased public awareness and a need to drive more incidences of self-referral. However, this was tempered by the inevitable impact of this on service demand.

Patient interviews

As stated previously, ten patients made contact to participate in the interview process of this project. Due to the small number of participants, it has not been possible to provide any regional/geographic break down of the interview outcomes without risking the potential identification of the participant and/or participating clinician. For this reason all the feedback provided has been aggregated and is reported on accordingly.
Referral route

As stated previously, patients were invited to contact Baccus Consulting to take part, and we had a positive response to this request from six women and four men. In line with the feedback from the participating clinicians, eight of those had been picked up in primary care, all as a consequence of a routine health screening. None of them attend clinics due to their own concerns regarding cholesterol levels or heart health and none of them as a consequence of the detection of high cholesterol in direct relatives. Two of those who participated were detected following significant cardiac episodes, both women, both under 45 at the time of the episode.

Family history

None of those who participated had had any indication of previous family links to suggest FH. Even for those who knew of deaths in the family due to CHD, they had not assumed any risk to them and none had had this suggested to them prior to the detection of their high cholesterol levels. Here there were insistences of family history of CHD and/or high cholesterol, participants did not consider themselves to be at risk and had not sought to self refer. All those with anecdotal family history considered that they were healthier than those affected family members and that they had taken steps to change habits and lifestyles, such as stopping smoking and/or losing weight.

Some of those who participated spoke of family estrangements where the detailed knowledge of a section of the family was unknown to them. All patients who participated stated that had they been made aware of any possible links to family history then they would have sought earlier testing.

One participant stated that despite a number of direct family members dying of “a heart attack”, including father, uncle and grandfather, it had not been suggested to them that they were at risk and this was only explored when the patient was found to have abnormally high cholesterol levels. Another patient said that on reflection they should have made the connection, but as none of the family doctors had done so, she thought she would be alright.

Genetic testing

Of those who participated, six had been diagnosed with FH following genetic testing, two had tested negative on genetic screening and a further two were awaiting the results of the genetic tests. Of the six who tested positive, all were subsequently followed up for cascade testing with direct family members invited to attend for testing.

There was a variation in how direct family members were contacted, with some having that initial contact made via the genetic clinical staff, some via the patient participant and some by a combination of both. Two participants who referenced family
estrangements were not in a position to either provide details or make contact with one or more direct family members.

Not all participants were fully aware if all contacted family members attended for testing and most reported that one, if not more, family members were unwilling to discuss the testing and its consequences. Of the six who tested positive resulting in cascade screening for direct family members, two were aware of direct family members who have subsequently been diagnosed with FH and a further two were aware of direct family members who are awaiting the outcome of subsequent tests.

However, all were offered genetic counselling with two of the six yet to have attended their initial counselling session. Those participants diagnosed with FH and testing positive at genetic screening who attended genetic counselling found the counselling to be on the whole positive and helpful, and one said that it helped her to rehearse what she would tell direct family members to help them respond to the cascade screening process.

All six participants diagnosed with FH and who tested positive said that the diagnosis had not so far had a detrimental effect upon their lives and for those who had previously reported, even anecdotally, a family history, it “made sense looking back”. Those who had a family history of CHD and/or high cholesterol all said that they had modified their lifestyle and that the diagnosis helped them to put those changes into the context of the diagnosis they had been given.

For those two participants still awaiting test results, both were aware that they met the Simon Broome criteria for FH and both fully expected that the result would be positive. It was not clear if either of them had been prepared for a negative result and each seemed to have self-determined the outcome of the genetic test.

The two other participants who met the Simon Broome criteria, but showed negative at genetic testing said that they felt uncertain about next steps for them. They both felt that they had made the necessary lifestyle changes, were adhering to statin therapy, but were uncertain of the impact of their circumstance on direct family members. One in particular had a history of anecdotal family history and was concerned that something had been missed. Both stated that their lipid clinic consultants had been supportive and helpful in terms of following up direct family members, but both said that the follow up had been difficult for them and one said that he could tell his son he should be tested, but not make him do it and he feared that he was now nagging him too much.

Summary of interviews with patients

- All came to lipid clinics via primary care, even where there had been previous cardiac episodes
- None reported previous abnormally high cholesterol in family members
Most seemed not to have considered themselves at risk despite previous family history of CHD/high cholesterol, including deaths.

Where patients tested positive at genetic testing stage, all were offered genetic testing and cascade screening for direct relatives.

In some cases patients followed up with direct relatives personally, some not at all and others a combination.

Not all patients were fully aware if all direct relatives had attended for cascade screening and/or had a positive diagnosis.

The issue of fractured families and disparate families would appear to present them some difficulties.

Those who tested positive were able to put the diagnosis into context.

Those who tested negative felt uncertain about the implication of this and the meaning of their elevated cholesterol.

And finally….

Patients participating were asked to comment on what they would like to see change, improve, and be done differently. Like the clinicians, all wanted to get across the message that FH is preventable and wanted to see increased public awareness and one patient said that more information should be made available when someone in the family has a heart attack, even if it is just encouragement to go to the doctor. One of the female patients wanted to see more information directed at younger women; saying that she thought she could not be affected because she was a woman in her 40s.

Conclusion

This section of the work has attempted to match the experiences of a small group of patients from across Scotland with the existing research literature. It is clear from both sections that there is scope for further work to be done with those patients who meet the criteria for FH, yet test negative at genetic screening. There was concern expressed by clinicians interviewed about the real and potential loss of significant numbers of these patients to the system.

Both clinicians and patients were clear that more awareness is needed and clinicians were also very aware that this would have an impact on already stretched resources, but both groups were at pains to point out that this is a preventable condition and the economic data clearly supports this assertion.
## Appendix 1

### Interview Schedule for Clinicians and Patients

| Q1. Are you male or female? – for patients only |
|---|---|
| Male | Female |

| Q2. What age are you? – for patients only |
|---|---|
| Younger than 20 | 20 – 30 |
| 31 – 40 | 41 – 50 |
| 51 – 60 | 61 – 70 |
| 71 – 80 | Older than 80 |

| Q3. When were you first diagnosed with FH? For patients only |
|---|---|
| In the last year | 2 – 3 |
| 3 – 4 | 4 – 5 |
| 5 – 6 | 6+ |

| Q4. Patients - Can you tell us about what led to you having your cholesterol tested? (tick all that apply) |

**Clinicians – route of referral**

- It was part of a general health test. Probe for details. E.g. check due to age? For medical insurance?

- I (patient) had concerns about my cholesterol levels.

- A family member/friend had concerns about my health.

**Clinicians – from secondary care**

| Q5. Were you aware of any family history prior to the test? For clinicians – ask about patients referred to them following positive test of direct family members. |
|---|---|
| Yes | |
| No | |
| □ Not sure/Don't know |  |
| □ Other |  |

**Q.6 Have any other family members been tested for high cholesterol since you were diagnosed with FH?**  
For clinicians – ask about referral process for direct family members for cholesterol testing.

| □ Yes | Who? |
| □ No | Why not? |
| □ Not sure/Don't know |  |
| □ Other |  |

**Q.7 Have any members of your family been offered (or had carried out) genetic testing since you were diagnosed with FH?**  
For clinicians – ask about ongoing referral for family members for genetic testing

| □ No | Why not? |
| □ Not sure/Don't know |  |
| □ Other |  |

**Q.8 How has the diagnosis of FH impacted on you and your family?**

Probe for:
- Diet
- Lifestyle
- Self esteem
- Paid work/unpaid work
- How other people see you
Appendix 2

Location of Lipid Clinics in Scotland

Inverness
Aberdeen
Dundee
Edinburgh x 2
Livingston
Falkirk
Stirling
Dumbarton
Glasgow x 4
Paisley
Ayr
Kilmarnock