British Heart Foundation

Cascade Testing Services for Familial Hypercholesterolaemia

Suzanne Sheppard is painfully aware of the devastation heart disease can cause.

Her father suffered a fatal heart attack in 1988 when he was 41 and she was just 15. His father had also died unusually young, due to a heart attack. This was the first clue that something wasn't right. Suzanne's cholesterol was twice normal levels. But no one could tell her why.

Thanks to the British Heart Foundation (BHF) part-funded pilot cascade testing programme in Wales, Suzanne finally found a reason for her high cholesterol; FH. With a single DNA test, one of the FH nurses identified that Suzanne had inherited a faulty gene which had caused her to have raised LDL cholesterol levels from birth. Her son, Cameron, has a 50/50 chance of inheriting the condition. He will be tested when he is ten.

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"FH cascade testing is more cost and clinically effective than most other models of care provided by the NHS."

Pears *et al*, 2014

Cascade Testing Services for Familial Hypercholesterolaemia

Summary

A cascade testing service for immediate relatives of people with familial hypercholesterolaemia (FH) has been successfully implemented in Wales and several countries in Europe. Life expectancy is improved by the optimal treatment of high cholesterol and other risk factors thereby reducing the risk of premature cardiovascular disease. The benefits are an improved outcome of individuals and families and a reduction in the costs associated with premature cardiovascular disease.

Evidence summary

YES The intervention has been successfully implemented

YES The intervention has been successfully replicated

YES The intervention is linked to NICE guidance and a NICE quality standard

YES The intervention is supported by several national organisations

YES An evaluation of the effects of the intervention has been carried out

YES There are publications relating to this intervention.

The Proposal

THE PROPOSAL	Improve quality outcomes for people with familial hypercholesterolaemia (FH) and reduce health and social care costs by reducing the person's risk of premature and avoidable cardiovascular disease through service improvement to improve detection, diagnosis and optimal therapy and management in both primary and secondary care.
PURPOSE OF CHANGE	To improve the identification, diagnosis, risk stratification and optimal management of people with FH to reduce risk of premature and avoidable cardiovascular disease.
TYPE OF CHANGE REQUIRED	National roll-out of FH cascade testing services supported by the relevant commissioning authorities in each nation. Health economic studies argue strongly in favour of systematic cascade testing to identify new FH patients using DNA testing for unambiguous identification of affected relatives. This method is used very successfully in other countries in Europe, notably Holland. Economic modelling has estimated that treatment of every 50,000 FH patients (between the ages of 30 and 85 years) with high intensity lipid-lowering statin therapy would lead to more than 5,000 fewer cardiovascular deaths when compared with no treatment.[1] **Children with FH** • There are approximately 13 million children under the age of 18 years in the UK and, based on current FH incidence rates, it is estimated at least 26,000 will have FH. Of these, the 2010 UK National FH audit reported that fewer than 400 had been identified and were receiving the appropriate care in clinics. • Based on published evidence, NICE guidance suggests all at risk children should be tested before the age of 10 years and that use of statins to reduce LDL cholesterol should be considered by the age of 10 years.[2] Cascade testing is an effective means of identifying at risk children and, with parental consent, relevant growth and health data of all identified children are being entered onto the RCP/RCPCH FH children's register, which is currently fully funded by the BHF and supported by HEART UK.
RELATED STANDARDS AND GUIDANCE	NICE Clinical Guideline 71: identification and management of familial hypercholesterolaemia. NICE 2008. NICE Quality Standard 41 (2013): Familial Hypercholesterolaemia. The NHS operating Framework 2012/2013 states: '2.16 In addition to the outcomes strategies, NHS organisations should continue to support other clinical strategies aimed at reducing early mortality from cardiovascular disease including heart disease, stroke, kidney disease and diabetes.' '2.17 There is strong evidence that early treatment supports better clinical outcomes. There are a number of key areas where commissioners and providers can work together to ensure earlier diagnosis and treatment.'
OTHER INFORMATION	Familial hypercholesterolemia, a high concentration of LDL cholesterol in the blood, is caused by a genetic defect that shows an autosomal dominant pattern of inheritance. This means that siblings and children of a person with FH have a 50% chance of inheriting the condition. The incidence of FH was previously thought to be 1 in 500, but the latest data from Denmark, the Welcome Trust and from BHF funded research suggests it could be as high as 1 in 200[3,4]. Based on this incidence rate, it is estimated there could be over 300,000 FH patients in the UK, but in most cases the condition is not recognised clinically. Less than 15% of FH cases are currently detected and treated in lipid clinics, and overall less than 5% of FH cases are properly diagnosed by genetic testing.[5] Systematic testing of first-degree relatives of patients with FH is significantly lacking in large parts of the UK. The Welsh FH service received pump-priming from the BHF in 2010 for specialist nursing input prior to full NHS funding. In March 2014, the BHF invested an additional £1million to set up cascade testing services in England and Scotland.
SAVING LIVES AND REDUCING COSTS	'Overall the potential savings to the UK are almost £380 million from coronary heart disease (CHD) events avoided if all relatives of FH index cases are identified and appropriately treated. More realistically, if 50% of patients with FH are diagnosed and treated, the NHS could save £1.7 million per year on health treatment otherwise required for CHD, but not implementing cascade screening is costing the NHS £1.4 million per year.'[6]

1 HEART UK. Saving lives, saving families. The health, social and economic advantages of detecting and treating familial hypercholesterolaemia (FH). Available from: http://heartuk.org.uk/files/uploads/HUK_SavingLivesSavingFamilies_FHreport_Feb2012.pdf [accessed November 2014].

2 National Institute for Health and Care Excellence. Clinical guidelines and evidence review for familial hypercholesterolaemia: the identification and management of adults and children with familial hypercholesterolaemia. London: NICE; 2008 (Clinical Guideline 71).

3 NordestgaardNordestgaard BG, Chapman MJ, Humphries SE, *et al*. Familial hypercholesterolaemia is underdiagnosed and undertreated in the general population: guidance for clinicians to prevent coronary heart disease. Consensus Statement of the European Atherosclerosis Society. *Eur Heart J* 2013; **34**:3478–90.

4 And Benn M, Watts GF, Tybjaerg-Hansen A, et al. Familial hypercholesterolemia in the Danish general population: prevalence, coronary artery disease, and cholesterol-lowering medication. *J Clin Endocrinol Metab* 2012; **97**:3956–64.

5 Pedersen KMV, Humphries SE, Roughton M, *et al*. The National Clinical Audit of the Management of Familial Hypercholesterolaemia 2010: Full Report. Clinical Standards Department, Royal College of Physicians, December 2010.

6 HEART UK. Saving lives, saving families. The health, social and economic advantages of detecting and treating familial hypercholesterolaemia (FH). Available from: http://heartuk.org.uk/files/uploads/HUK_SavingLivesSavingFamilies_FHreport_Feb2012.pdf.

Evidence of Implementation

ORGANISATIONS WHERE THE PROPOSAL HAS BEEN IMPLEMENTED	NHS Wales (part-funded by the BHF from 2010 to 2013).
SERVICE DESIGN & APPROACH	Several factors have contributed to the success of the Welsh FH service: • A joined up approach between different parts of NHS Wales – including primary and secondary care. • The All Wales Medical Genetics Service infrastructure combined with the facility to coordinate laboratory genetic testing. • Leadership from the Cardiac Networks and Lipid Clinic consultants. • University Wales Gene Park support for pilot research projects. • Powerful interest from local patient groups, strongly supported by the Genetic Alliance, HEART UK and the British Heart Foundation (BHF). The British Heart Foundation (BHF) recognised that Wales is an exemplar for this approach to cardiovascular disease prevention and partnered with the Welsh Government, to fund FH clinical nurse specialists for the first 3 years of the service. Service implementation commenced in 2010 with clinically led patient pathway creation, laboratory testing and IT system development. The service which is hosted by the All Wales Medical Genetics Service is now successfully operating within a multidisciplinary setting. FH specialist nurses working with Lipid Clinic consultants, designated Cardiologists and Paediatricians across Wales, act as gate keepers for FH genetic testing for patients referred with hypercholesterolaemia. The service has developed clinical scoring criteria that allow DNA testing to be targeted in a cost-effective manner. The cascade testing for affected families is carried out by genetic counsellors.
EFFECT ON QUALITY OF CARE	**Safety** • Improved detection of index cases with FH (first person in the family to be identified with FH) in Primary Care. • Improved detection of other family members with FH. • Improved quality outcomes for people with FH through optimal therapy to reduce risk of premature cardiovascular disease. **Effectiveness** • Cost-effective treatment for FH (with statins) and other CVD risk factors (particularly smoking), reduced risk of premature cardiovascular disease and avoidance of health and social care costs from cardiovascular disease due to untreated FH. • Improved productivity through a reduction in referrals and bed days saved through prevention of premature cardiovascular disease and heart attack. **Patient experience** Prevention of premature and avoidable mortality from FH related premature cardiovascular disease. FH can cause cardiovascular disease as young as 30 years old – in some families it can lead to multiple premature deaths through generations. The confirmation of absence of disease also brings benefits for family members.
IMPACT ON REDUCING MORBIDITY AND MORTALITY	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. However, early treatment with lipid lowering drugs can increase life expectancy to near the average for the non-FH population.[7]
TIMESCALES FOR REALISATION OF BENEFITS	Index patients can be assessed and genetically tested within 4-6 months. Family testing for the family mutation can then proceed within 4-12 months of the index patient being diagnosed using a DNA test.
ADDITIONAL COSTS	Additional costs incurred include costs associated with genetic testing, an IT support system, managerial and clerical support.
EVIDENCE FOR THE EFFECT ON QUALITY AND PRODUCTIVITY	Further information relevant to the Welsh FH service can be found online at the website below: http://www.fhservice.wales.nhs.uk/research-publications-from-fh-wales

Evidence on replication

EVIDENCE ON REPLICATION	Yes in the NHS - Northern Ireland, some areas of Scotland and some areas of England have introduced genetic testing and family cascade testing. Yes International – particularly in the Netherlands In addition to the Wessex FH Cascade Testing service outlined below, there are 7 BHF part-funded FH services currently being set up in England and Scotland and hosted in the following NHS Trusts: • The Royal Brompton and Harefield NHS Trust, England • The Royal Free London Foundation NHS Trust, England • Sheffield Teaching NHS Trust, England • Central Manchester Foundation Trust, England • University Hospital Bristol, England • City Hospitals Sunderland, England • NHS Grampian, Scotland
DETAILS OF REPLICATION	The Wessex Familial Hypercholesterolaemia Cascade Testing Service has been established to raise awareness, identify and manage people with FH and provide a high quality genetic cascade testing service at a regional specialist level. This service is the first to be commissioned by CCGs in England. The service is being hosted by the Wessex Clinical Genetic Service based at University Hospital Southampton Foundation Trust and has been pump primed by the South Central Cardiovascular Network (SCCVN). It is supported with BHF funding for an FH nurse.
SERVICE DESIGN AND APPROACH	A dual primary and secondary care pathway was agreed by key stakeholders. The rationale for this pathway was to optimise the identification of people with FH by allowing equal access to the Wessex FH Cascade Testing Service from primary, secondary and tertiary care. A shared care approach is described for the diagnosis and management of FH patients with an ongoing dialogue between primary and secondary care with specialist advice as and when required. The justification for this is that it not only raises awareness across primary, secondary and tertiary care but also limits unnecessary referrals into secondary care maintaining quality of care at the same time as cost effectiveness. For example; within the West Berkshire region the Consultant Lipidologist has established a virtual lipid clinic through the 'Choose & Book' system whereby GPs are encouraged to discuss the diagnosis and management of patients with a possible diagnosis of FH.

7 Neil A, Cooper J, Betteridge J, Capps N, McDowell I, Durrington P, Seed M, Humphries SE. Reductions in all-cause, cancer, and coronary mortality in statin-treated patients with heterozygous familial hypercholesterolaemia: a prospective registry study. Eur Heart J. 2008 Nov;29(21):2625-33.

> My son has a 50/50 chance of having FH... because we've got cascade testing he will be tested early and treated if necessary. That's given me peace of mind.
>
> Suzanne Sheppard

Further evidence

INTERNATIONAL PAPERS	Ademi Z, Watts GF, Pang J, Sijbrands EJ, van Bockxmeer FM, O'Leary P, Geelhoed E, Liew D. (2014) Cascade screening based on genetic testing is cost-effective: evidence for the implementation of models of care for familial hypercholesterolemia. J Clin Lipidol 8(4):390-400 HEART UK – The Cholesterol Charity: Systematically identifying familial hypercholesterolaemia in primary care; An audit within the Medway Clinical Commissioning Group. Available from heartuk.org.uk Nherera L, Marks D, Minhas R, Thorogood M, Humphries SE. (2011) Probabilistic cost-effectiveness analysis of cascade screening for familial hypercholesterolaemia using alternative diagnostic and identification strategies. Heart. 2011 Jul;97(14):1175-81 Nherera L, Calvert NW, Demott K, Humphries SE, Neil HA, Minhas R, Thorogood M. (2010) Cost-effectiveness analysis of the use of a high-intensity statin compared to a low-intensity statin in the management of patients with familial hypercholesterolaemia.Current Med Res Opin. Mar;26(3):529-36 Pears R, Griffin, M, Watson, M, et al. The reduced cost of providing a nationally recognised.service for familial hypercholesterolaemia. *Open Heart* (2014) BMJ.com. Watson M (2010) Exploring the impact of DNA testing for familial hypercholesterolaemia. *British Journal of Cardiac Nursing*. 5 (Pt 6) 293-298.
SUPPORT FROM NATIONAL ORGANISATIONS	The British Heart Foundation HEART UK – The Cholesterol Charity The National Institute for Health and Care Excellence

Implementation advice

IMPLEMENTATION GUIDANCE	While a diagnostic genetic (DNA) test is more expensive than a cholesterol test alone, its use significantly improves the cost effectiveness of cascade testing and is strongly recommended in NICE Clinical Guidance 71 on FH and in the NICE Quality Standard for FH. With the introduction of next-generation sequencing technologies and use of simultaneous targeted sequencing of all three FH-causing genes, the cost of testing an index case is reducing, making the use of DNA diagnosis even more cost effective. There are several accredited genetic diagnostic laboratories in the UK that offer such a service and commissioners should consider combining service bids to negotiate best value where high sample volume can be guaranteed.
IMPLEMENTATION CHALLENGES	The BHF has identified that one of the biggest barriers to implementation of FH cascade testing services is the difficulty service providers experience in securing funding for genetic tests. It is imperative that both service providers and commissioners understand the true costs of delivering an FH cascade testing service and the benefits it brings both in improving patient outcome and the associated reduction in costs to the NHS.
TOOLS TO SUPPORT IMPLEMENTATION	FH Toolkit, HEART UK, available from heartuk.org.uk FH Business Case Template available from bhf.org.uk/fhfunding
KEY CONTACTS	**British Heart Foundation** Jo Whitmore, FH Clinical Lead whitemorej@bhf.org.uk **HEART UK** Helen Walsh, Campaign & Public Affairs Manager hw@heartuk.org.uk
OTHER CONTACTS	**Clinical Leads and FH Nurses for each BHF funded FH Service:** **Royal Brompton and Harefield NHS Trust** Clinical lead: Dr Mahmoud Barbir (m.barbir@rbht.nhs.uk) FH nurses: Emma Neves (e.neves@rbht.nhs.uk), Lorraine Priestley-Barnham (l.priestley-barnham@rbht.nhs.uk) **Royal Free London NHS Foundation Trust** Clinical lead: Darren Harvey (darren.harvey@nhs.net) **Sheffield Teaching NHS Trust** Clinical Lead: Dr Nigel Wheeldon (nigel.wheeldon@sth.nhs.uk) FH nurses: Alison Moore (alison.moore2@sth.nhs.uk), Michelle Tyler (Michelle.Tyler@sth.nhs.uk) **Central Manchester Foundation Trust** Clinical Leads: Dr Handrean Soran (handrean.soran@cmft.nhs.uk), Ruth Eatough (ruth.eatough@cmft.nhs.uk) FH nurse: Rebekah Swan (rebekah.swan@cmft.nhs.uk) **University Hospitals, Bristol** Clinical Lead: Dr Graham Bayly (graham.bayly@uhbristola.nhs.uk) FH nurse: Lisa Gritzmacher (lisa.gritzmacher@uhbristol.nhs.uk) **City Hospitals Sunderland** Clinical Lead: Dr Dermot Neely (dermot.neely@nuth.nhs.uk) **North of Scotland Cardiac Network, NHS Grampian** Clinical Lead: Prof Zosia Miedzybrodzka (zosia@abdn.ac.uk) **University Hospital Southampton** Clinical lead: Melanie Watson (melanie.watson@uhs.nhs.uk) FH nurse: Darren Alderson (darren.alderson@uhs.nhs.uk)

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