Strategy for Implementation of NICE FH Guideline in the North East SHA

Summary

This paper describes a proposed development within the North East SHA involving the regional genetics service and existing specialist lipid clinics, to provide a patient centred service for familial hypercholesterolaemia (FH) which would allow optimal compliance with the NICE guideline (CG71): "Identification and management of Familial Hypercholesterolaemia", published in August 2008. The proposed service will involve a multidisciplinary approach which would identify 90% of the estimated 5000 undiagnosed FH cases in the region within 6 years. Primary care and cardiology services would refer suspected FH cases to the specialist lipid clinics for assessment and entry into a regional care pathway for DNA Diagnosis and Family Cascade Testing if the clinical diagnosis of FH is confirmed. Affected family members identified by cascade testing will be referred to a lipid clinic within the SHA wide network for assessment and initial management, with an ongoing management plan agreed with primary care.

Introduction

Familial Hypercholesterolaemia (FH) is an inherited metabolic disorder with an estimated population prevalence of 1 in 500 in the UK, or approximately 6000 cases in the North East, of whom probably less than 1000 have been diagnosed. In affected individuals, concentrations of harmful (atherogenic) LDL-cholesterol in the blood are typically doubled from birth leading to early development of advanced atherosclerosis. Without treatment, affected men will frequently develop symptoms of coronary heart disease before 40 years and half will be symptomatic by the age of 50 years. In women a similar proportion are symptomatic by 60 years. The clinical expression of FH is affected by dietary and lifestyle factors and those with FH living in the North East may do particularly badly as the problem is exacerbated by the high content of saturated fatty acids in the diet and the high prevalence of smoking.

Individuals with FH have an alteration in a gene, inherited as an autosomal dominant trait which means that each of their first degree relatives (parents, siblings and children) have a 50% chance of also being affected. The NICE FH Guideline recommends genetic testing of relatives of individuals known to have FH which is the most effective strategy for early identification of affected individuals, leading to effective treatment through diet, lifestyle interventions and cholesterol lowering drugs. With early intervention and careful follow up to ensure concordance with treatment the excess coronary heart disease risk and premature mortality associated with FH can be effectively eliminated.

Key Recommendations in the NICE FH Guideline

The guideline contains recommendations on the identification individuals with FH and their relatives using cascade testing and their subsequent management which define the implementation strategy and are reflected in the audit standards:

- Healthcare professionals should consider the possibility of FH in adults with raised cholesterol (total cholesterol typically greater than 7.5 mmol/l), especially when there is a personal or a family history of premature coronary heart disease. [1.1.1]
- All individuals with FH should be referred to a specialist with expertise in FH for confirmation of diagnosis and initiation of cascade testing. [1.2.2]
• Cascade testing using a combination of lipid concentration measurement and DNA testing should be used to identify relatives of index cases with a clinical diagnosis of FH. [1.2.4]
• Children and young people diagnosed with, or being investigated for a diagnosis of, FH should be referred to a specialist with expertise in FH in an appropriate child focused setting. [1.3.1.14]
• All individuals and families with FH should be offered individualised nutritional advice from a healthcare professional with specific expertise in nutrition. [1.3.2.2]
• Prescription of a potent statin should usually be considered when trying to achieve a reduction of LDL-C concentrations of greater than 50% (from baseline). [1.3.1.2]
• All treated individuals with FH should have a regular structured review carried out at least annually. [1.5.1.1]

Proposed Regional Strategy and Care Pathway

The proposed strategy is to build on the existing strengths of Northern Genetics Service (NGS) and the established Specialist Lipid Clinics to implement the Guideline according to the following 5 step care pathway (See Appendix 1, Model 1):

1. Clinical assessment - for entry into the FH Cascade Testing Pathway
2. DNA Diagnosis (genotyping)
3. Cascade Testing in Families (based on genotype where possible)
4. Clinical management
5. Long term follow up – annual structured review

Northern Genetics Service to undertake steps 2 and 3 and steps 1, 4 and 5 the would be undertaken by the nine Specialist Lipid Clinics already established within the SHA (Table 1) with the future development of nurse led and primary care based follow up arrangements.

Assessment for DNA Diagnosis and entry into FH Cascade Testing Pathway. New patients suspected to have FH are likely to arise in primary care and cardiology services who will refer patients to the specialist lipid clinics for assessment and confirmation of diagnosis of FH. Initiation of DNA based family cascade screening involves the commitment of significant clinical and laboratory resources and the Specialist Lipid Clinics would ensure only appropriate cases enter the pathway. Unlike NGS, at present the Specialist Lipid clinics are not a regional service but have operated for some years as a cohesive group in an informal educational network (Northern Lipid Forum). All are capable of meeting the NICE Guideline standards and all have expressed a willingness to operate as a regional Lipid Specialist Network (LSN) aligned to the regional Cardiovascular Network, to accommodate additional referrals and to adhere to a common care pathway for clinical assessment and management of FH, including the use of generic statins where possible and appropriate use of more potent non-generic statins only where required.

Additional capacity in Specialist Lipid Clinics. It is proposed that the additional referrals and follow up appointments are accommodated by expansion of the capacity of the Specialist Lipid clinics participating in the LSN and the additional activity commissioned locally at standard outpatient tariff. The standard outpatient tariff should cover all the assessment costs in clinic, excluding DNA diagnosis (genotyping) however the additional time in clinic for counselling and explanation of DNA diagnosis and Family Cascade Testing will not. One solution to this would be to have regionally based nurses in attendance at clinic sessions.
when FH cases are booked in for assessment. This would also provide a useful co-ordinating link role to NGS.

**DNA Diagnosis (genotyping).** Family cascade testing can be undertaken using total or LDL-cholesterol but there is considerable overlap between measured levels in affected and unaffected individuals leading to “grey” cases where uncertainty remains. Identification of a causative DNA mutation in a family provides a clear diagnosis and identification of relatives with a minimum of uncertainty. At present cascade testing based on DNA diagnosis has only been carried out on a research basis in England. The Newcastle Lipid and Metabolic Clinic, in collaboration with NGS, has been one of 5 UK centres involved in the Department of Health sponsored FH cascade testing research project from 2005 to 2008 during the course of which 145 FH families from the Newcastle clinic were tested. As a result of this work a bank of DNA samples has been established to facilitate the development of DNA genetic testing and considerable experience has been gained in family cascade testing in FH based on both DNA results and LDL-cholesterol.

**Family Cascade Testing.** NGS is therefore best placed to offer DNA diagnosis and cascade testing as this is part of their routine work and genetic health professionals are well versed in the ethical and family dynamic issues that may arise. It is proposed that the genetic component of the strategy (clinical and laboratory) should be commissioned through specialist commissioning and could include an expansion of the regionally based Cardiovascular Genetics Specialist nurses to provide sessional support for the Specialist Lipid clinics on an outreach basis (Model 2, Appendix 1) where patients and/or relatives are unable to travel to a Genetics Centre. The pilot project (described above) has established a benchmark rate for positive DNA diagnosis and number of affected relatives identified per index case which will be used to assess the performance of the Lipid Clinics in selecting appropriate cases for Family Cascade Testing.

**Development of awareness in primary care and long term follow up.** Working in conjunction with NGS are GPs with a special interest (GPSI) in Genetics who have established an excellent network to provide education, support and updated information for GPs to enable them to make appropriate referrals to the specialist clinics. Once the pathway is established it is proposed that the LSN would play a role in developing and encouraging increasing involvement of primary care based staff including but not limited to GPSIs in the clinical management and long term follow up of FH.

**Benefits of Preferred Option**

This proposal would enable all PCTs within the SHA to ensure compliance with the NICE guideline. This initiative would also be in line with the North East Region Public Health strategy “Better Health, Fairer Health” under the “Preventing ill health and working to improve health and wellbeing” element. At present, some patients with FH are already being treated in specialist clinics, some are being treated empirically in other clinics and primary care is suboptimal for other family members in whom diagnosis is unnecessarily delayed. An ad hoc service will inevitably lead to avoidable, premature, cardiovascular deaths. The proposed service will provide a means of achieving equity of service provision across the SHA. Spending resources on a FH service will save on the long term acute and primary care costs for a patient following a CVD event and the cost of caring for a patient undergoing revascularisation procedures.
Summary of Costs

For a 3 year summary of costs see Appendix 2

Risk Analysis of Preferred Option

The proposed service has already been in operation in the Newcastle as part of national pilot study\(^3\). Among the 5 participating centres Newcastle achieved the highest clinical pick-up rate of genetically confirmed FH and the highest rate of identification of relatives on cascade testing.

The NICE guideline 1.2.8
“the establishment and use of a nationwide family based follow-up system is recommended to enable comprehensive identification of affected individuals”\(^1\). If a FH service is not developed the NICE guideline will not be supported in the North East and care of patients will not be in line with the national public health strategy. This will become a performance issue for the SHA.

Timescales for Implementation

Establishment of lipid clinic network Winter 2008
Laboratory preparatory work Spring 2009
Education of GPs Spring 2009
Roll out of service April 2009

Appendices

Appendix 1 Model Care Pathways
Appendix 2 Summary of costs

References

1. NICE Guideline (CG71): Identification and management of Familial Hypercholesterolaemia
2. Regional Strategy www.go-ne.gov.uk/gone/public health/?a=42496
3. FH cascade project www.fhcascade.org.uk
Appendix 1 Proposed Care Pathways.

Model 1 - Genetics Centre Based

Model 2 - Outreach Service
Appendix 2. Summary of Cost Estimates

<table>
<thead>
<tr>
<th>Activity</th>
<th>Annual activity</th>
<th>Year 1 09-10</th>
<th>Year 2 10-11</th>
<th>Year 3 11-12</th>
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<td>New “suspected FH” referrals</td>
<td>450</td>
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<td>Non-recurrent costs for DNA Diagnosis</td>
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<td>Recurrent costs for DNA Diagnosis &amp; CT</td>
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<tr>
<td>- Cascaded and genotyped</td>
<td>300</td>
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<tr>
<td>- mutation positive</td>
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<tr>
<td>- Relatives tested for mutation</td>
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<tr>
<td>- mutation positive relatives referred</td>
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<td>- mutation negative</td>
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<tr>
<td>- mutation negative relatives referred</td>
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<td>New referrals at tariff of £208</td>
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<td>Pre-test counselling x 300 = 100 days Cardiovascular Genetics nurse time</td>
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<td>300 25 k 25 k 25 k</td>
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<td>Initial Treatment reviews at tariff £103</td>
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<td>Structured reviews (Year 2) at tariff £103</td>
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<td>Cumulative Number of cases diagnosed</td>
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<td>Treatment costs (NICE Estimate)</td>
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<td>Cost savings (NICE Estimate)</td>
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<tr>
<td>Total Costs</td>
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* Assumes atorvastatin comes off patent in Q3 2011
** Additional 75k added each year to annual costs of structured reviews Y4 –6
*** Treatment costs expected to fall by >50% after Y4
**** Paediatric outpatient costs will apply in approx. 10-20% of relatives but less frequent structured reviews may be required