UK NATIONAL SCREENING COMMITTEE

Policy Review

Screening for Familial Hypercholesterolaemia

17 November 2011

Aim

1. To agree the UK National Screening Committee's (UK NSC) formal policy position on screening for familial hypercholesterolaemia (FH).

Background

2. A review of screening for FH against the UK NSC criteria for appraising the viability, effectiveness and appropriateness of a screening programme was carried out earlier this year by Dr Anne Mackie, Steve E Humphries and H Andrew W Neil (on behalf of the Simon Broome Register Committee).

3. The review concluded that full population screening for FH in adults does not seem on the balance of available evidence to fulfil the criteria for a screening programme.

Consultation

4. A copy of the review of screening for FH against the UK NSC criteria was placed on the UK NSC website for consultation for three months. The consultation closed on 30th September 2011. A copy of the consultation replies are available at Annex A.

Recommendation

8. The UK NSC is asked to agree the policy position on screening for FH as follows:-

A national screening programme for FH is not recommended.

9. The UK NSC is asked to agree that the policy should be reviewed in three years time unless there is significant new peer reviewed evidence in the meantime.

Annex A

Consultation Replies

Dr Trevor Cole MB ChB FRCP
Consultant in Cancer and Clinical Genetics and Chair of the JCMG

Birmingham Women's NHS
NHS Foundation Trust

WEST MIDLANDS REGIONAL CLINICAL GENETICS SERVICE

Clinical Genetics Unit
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Please quote our reference on all correspondence: TC/as/77
Date: 14 July 2011

Anne Mackie
Chairman of the National Screening Committee
UK National Screening Committee
Imperial College Healthcare NHS Trust
Mint Wing, Centre Block G
South Wharf Road
London, W2 1NY

Dear Anne

RE: Screening for Familial Hypercholesterolaemia

Thank you very much for forwarding the National Screening Committee document on Familial Hypercholesterolaemia in adults to the JCMG.

As I am sure you would suspect, the JCMG strongly supports the NICE clinical guideline 71 on identification and management of Familial Hypercholesterolaemia using cascade surveillance. The evidence of benefit, including the cost per qualy, strongly seems to support this approach.

It is of some disappointment to the JCMG that while the molecular testing has been funded in the three devolved countries, such funding has been difficult to identify across England, such that the distribution of the service is in practice very limited.

It is also of concern to the JCMG that the current method of cascade screening through lipid clinics has, as yet, only identified a very small proportion of those believed to be at risk. This is a situation which certainly is not helped by the limited availability of molecular testing; something of a "chicken and egg" scenario.

At the current time a small number of laboratories are developing kits or using commercial kits to identify common LDL receptor mutations plus a small number of mutations in other genes (APOB and PCSK9).

Despite FH molecular kits becoming more bespoke, they still will fail to detect a proportion of at risk individuals within the community. Of particular concern is that the mutation spectrum may well not reflect that identified in minority ethnic groups. As such, testing may be an additional mechanism compounding inequalities of service to these groups.

The most appropriate form of molecular testing also needs to be considered, in light of the disappointing figures alluded to above, the potential future changes in the field of molecular biology and the additional cost that would occur if incomplete testing were undertaken at the current time. It would add significant clinical, administrative and laboratory costs if families had

to be re-contacted for repeat testing by next generation sequencing as this becomes widely available in the near future..

I believe it would be important that the National Screening Committee therefore considers the ongoing assessment being undertaken by the NICE Diagnostics Committee which I believe is now out for public comment.

It appears that the evidence that will emerge is that although the current cost of comprehensive genetic analysis compared to the kits is higher, the overall cost per qualy is still extremely good value for money and the additional benefit from detection rate justifies a more comprehensive approach.

The JCMG will certainly await with interest the final deliberations of the National Screening Committee and hope that this in itself may provide a useful additional lever with Commissioners to take this very worthwhile programme forward.

Yours sincerely

Dr Trevor Cole MB ChB FRCP
Consultant in Cancer and Clinical Genetics
And Chair of the JCMG

CC:

Anne Cecile Ville
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Professor Adrian Newland
Chairman
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Simon Land
Royal College of Physicians

Dear Anne

Please take this email as confirmation that the Royal College of Physicians wishes to endorse the comments submitted by Dr Trevor Cole (Chair of the JCMG) with relevance to this consultation. I would be grateful if you could confirm receipt.

Best wishes
Simon

Dr Alan Fryer
Consultant Clinical Geneticist
Royal Liverpool Children's Hospital (Alder Hey)

As a clinical geneticist in Mersey region we see few cases of FH and when we do get referrals we pass them to our colleagues in lipid clinics. Our lab set up DNA testing but the numbers of samples received has been low - partly this is a funding issue and partly because some lipid clinic doctors feel that DNA testing does not add much to cholesterol levels. I am not clear from the NICE guidance if the authors were advocating DNA testing for both definite or possible FH cases or just the definite cases on the Simon Broome criteria???

A big issue for lipid clinics is cascade screening - our colleagues in these clinics have been seeking funding but I suspect they are struggling.

Reply from Dr Mackie

Thanks for your comments. I assume you mean that you're content that the recommendation remains as cascade screening rather than population screening but that cascade screening isn't terribly effective?

Further response from Alan Fryer

As a clinical geneticist we are very much geared towards cascade screening and it seems a sensible approach compared to population screening. My comment was that some of our lipid clinics are not geared to offering cascade screening and do not/have not achieved the funding to develop it. It could be very effective if there was adequate funding and training.

Dr Christine Patch
Chair
British Society for Human Genetics

Dear Dr Mackie

The British Society for Human Genetics strongly supports early case identification and appropriate treatment in familial hypercholesterolaemia. There is acceptance across the world that there is health benefit from early identification of cases and subsequent adequate treatment. There is evidence that cascade testing in families and appropriate DNA based diagnostic testing is cost effective. We wait for the outcome of the development of diagnostic guidance from NICE as to the methods of molecular analysis.

As noted in a preliminary report from this group the NICE clinical guideline 71 identified DNA testing as the recommended method for confirming a clinical diagnosis of FH among people with a possible or definite diagnosis and allowed for accurate identification of cases amongst relatives. It is disappointing that the 2010 audit of FH services suggest that these recommendations are not being widely implemented. This audit found that 97% of sites have access to an accredited laboratory for lipid measurement, but only 15% have access to funded DNA testing.

As the cost of comprehensive genetic analysis comes down the cost effectiveness of DNA based approaches to diagnosis and cascade testing can only improve. There are undoubtedly barriers to implementation which include funding for molecular testing. It is extremely disappointing that, despite this strong evidence, family screening is not yet happening across the UK.

Dr Devaki R Nair
Consultant Clinical Biochemistry
Royal College of Pathologists (SAC in Clinical Biochemistry)

Familial hypercholesterolaemia in UK is hugely under diagnosed in spite of this condition being recognised as an important health problem. To date, few commissioners have taken action and FH remains something of a “Cinderella” condition. When diagnosed, FH can be effectively treated with statins. It is estimated that if the detection rate for FH was improved to 80-90%, the potential saving to the NHS in terms of reduced premature morbidity/mortality would be of the order of £20m. The expert review recommends cascade screening to allow cost-effective primary prevention interventions and accepts that this is not implemented effectively as recommended. Resources for this activity has not been identified for the primary care or secondary care organisations with reference to staff required to screen the relatives and also the cost to the clinical biochemistry departments for the additional tests that may be required. Unless resources are identified this problem will continue and FH will remain to be under diagnosed. It is not practical for the primary care to organise cascade screening as a number of relatives who need to be tested may live outside the territory where the index patient is seen. Specialist centres can develop the capacity by training a multidisciplinary team including nurses and health care assistants to work alongside the primary care team and the lipid specialists.

Although it has been shown that DNA testing has not indicated any major impact on psychosocial problems during the UK RCT trial, the support provided may not be available if DNA testing is rolled out to all specialist clinics if appropriate support for counselling is not provided.

Resource issues have also been the reason for not accessing the DNA test that can identify the mutation and confirm a diagnosis of FH in spite of the possibility of identifying a mutation in 80% of cases and the test being available in many accredited UK laboratories. The National audit on FH (RCP) confirms this problem.
Lack of data for cut points for certain population such of South Asian ethnicity should be recognised as the levels from Simon Broome criteria may not apply to this population.

Many patients with suspected FH may already be on a statin for a considerable period thus a diagnosis may not be considered in these subjects. It is unlikely the these subjects may have any tendon xanthoma as they have been treated with a statin from young as per the earlier CVD prevention programme by intervening a single elevated risk factor i.e. T cholesterol >8mmol/L . It is unlikely that these subjects would then be picked up for cascade testing. This gap in screening family members of FH has not been recognised.

The expert review recognises that it is important to distinguish polygenic hypercholesterolaemia and possible FH, the only way being offering genetic testing. The possibility of identifying a mutation in this group is much lower increasing the cost. Prioritising the subjects with definite FH to improve cost effectiveness of DNA testing is likely to widen the gap in management of those with a diagnosis of possible FH and may have a mutation if offered DNA testing. Specialist clinics with the necessary skills are more likely to make an appropriate decision to offer DNA testing and the expert review considers that this condition should be managed by lipid specialist.

There is also a difference in cost of genetic testing depending on the centre where it is offered and also depending on whether a complete screen or partial screen is available and this will complicate commissioning the service. If we are to aim for a national register uniformity in the offered tests and pricing is important. The review considers this difference but does not include recommendations.

The NHS Health check includes recommendation to consider a diagnosis of FH in people with a cholesterol concentration above 7.5mmol/L, but the success will depend on appropriate referral to the specialist. Some programmes do not include a cholesterol measurement and some programmes are provided by non NHS agencies without the results being updated on the GP system thus missing the opportunity to increase the pickup rate.

Unless this service is commissioned, for both cascade screen and DNA testing the guidelines and expert review as this is unlikely to impact on the total number of FH screened. It is important the laboratories, both the routine and the genetic labs are involved in this process from the beginning.

Dr Mike Knapton
Associate Medical Director – Prevention and Care
British Heart Foundation

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30 September 2011

Response to consultation on the UK NSC policy on familial hypercholesterolaemia screening in adults

The British Heart Foundation (BHF) is the UK's leading heart charity. We are fighting against heart and circulatory disease – which is the UK's biggest killer and claims over 180,000 lives each year.[1] We have been funding research into familial hypercholesterolaemia (FH) for over 25 years. We welcome the opportunity to respond to this consultation.

We support the recognition in the expert review document that cascade screening is the best way to increase the identification of unidentified cases of FH in family members of those living with this condition. The BHF is calling for national cascade screening in each of the four nations of the UK and in England, for this to be commissioned through NHS Specialised Services. Such national programmes need to be accompanied by an integrated national infrastructure of lipid clinics, genetic diagnostic services and establishment of a national patent register. There also needs to be investment in training for healthcare professionals to help them identify undiagnosed cases of FH and to support the families of people living with FH.

We agree that the NHS Health Check programme may help to identify some undiagnosed cases of FH in England. However, it is inevitable that only some patients in the target group will attend their appointment and important to note that the checks only cover people aged between 40 and 74. This is too late as FH affects people in younger age groups and 20-39 year olds living with undiagnosed FH have a 100-fold increase in their risk of dying from heart disease if they do not receive timely treatment[2]. A cascade screening programme therefore remains necessary and effective way of avoiding premature mortality from coronary heart disease..

Yours sincerely

Dr Mike Knapton
Associate Medical Director – Prevention and Care

[1] www.heartstats.org
[2] Scientific Steering Committee on behalf of The Simon Broome Register Group (1999) Mortality in treated heterozygous familial hypercholesterolaemia: implications for patient management. Atherosclerosis 1999; 142:105-12

Alastair Kent OBE, Director & Nick Meade, Policy Analyst
Genetic Alliance UK

UK National Screening Committee

Screening for familial hypercholesterolaemia in adults in the UK and the UK NSC screening criteria

Response from Genetic Alliance UK

Genetic Alliance UK

Introduction

Genetic Alliance UK is the national alliance of patient organisations representing families and patients affected by genetic conditions.

Since 2006, Genetic Alliance UK has worked to secure an all-Wales cascade screening service for familial hypercholesterolaemia (FH) within the NHS. We worked alongside over 70 individuals and families affected by FH who live in Wales, and alongside health professionals (clinicians, genetic counsellors, laboratory scientists and nurses) from a range of specialities (biochemistry, endocrinology, general practice and paediatrics) leading the campaign for a comprehensive diagnostic service.

In December 2010, the Welsh Assembly Government announced it was funding (in association with the British Heart Foundation) a cascade screening service for FH in Wales. This flagship NHS service is now in place. Index patients are being identified and their at-risk relatives are being screened using family pedigree assessment, blood cholesterol levels (according to the Simon Broome criteria) and genotyping. This clinical service is overseen by a multi-stakeholder steering group and is developed in accordance with best-practice clinical evidence, including the NICE guideline (clinical guideline 71 published August 2008).

We are grateful for the opportunity to respond to this consultation.

Cascade screening for familial hypercholesterolaemia

The evidence in favour of a UK National Screening Committee recommendation for a cascade screening programme for FH has been mounting for many years.

Previous to the full commissioning of the all-Wales service, a smaller-scale pilot had been underway in south east Wales. Both this earlier implementation and the present service should be seen as pilots of a scheme for the United Kingdom, informing health service planners and providers of an effective way of delivering this service for primary prevention of coronary heart disease. The success of the programme in Wales should be built on and its developmental issues learnt from.

This programme certainly indicates that a national cascade screening programme for FH is both feasible and beneficial to the 1 in 500 people affected by the condition, to benefit their health and well-being; cascade screening for this inherited condition can give a clear diagnosis, allowing for effective management with lifestyle modification and cholesterol-lowering medication.

Programmes have also been running in other European countries for a number of years. Each programme takes a differing approach, and can be examined for evidence and indication of the best strategy for UK health services.

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The NICE CG71 full guideline on FH, published in 2008 recommended cascade screening. This document has now been cited across the world as evidence that a cascade screening programme is the best practice strategy for identifying FH patients.

The strongest case for a UK FH screening programme is given by the simple facts that: FH is a common condition, untreated affected FH patients develop coronary heart disease and are at significant risk of premature death, however the condition can be effectively diagnosed, managed and treated.

On the basis of the evidence presented in the document under consultation, and the evidence above, Genetic Alliance UK is convinced that a national screening programme for FH should be implemented in all UK health services as a matter of priority.

Specific comments on the consultation document

The title of this review excludes children. The basis of this exclusion is not explained in the document. As the document states, NICE guideline CG71 suggests that children should be tested by the age of 10 years. Genetic Alliance UK proposes a broadening of the scope of this document to take account of the NICE guidelines and include children and young people.

The answer to question 9 explains significant cost savings that can be gained by implementing a commercially available test for the most common FH mutations. If a screening programme was to be launched based on this document, we believe there should be a commitment to review the relative cost of a full gene screen on a frequent basis, to ensure a full gene screen is implemented as soon as it is cost effective.

Question 12 identifies the need for increased capacity in lipid clinics and states there is limited access to DNA testing. We believe the specific need for capacity building in regional genetic services should be explicitly stated here. Additionally the need for capacity building in paediatric services should also be recognised.

Question 21 discusses NHS Health Check in relation to full population screening for FH. While Genetic Alliance UK continues to believe cascade screening is the most appropriate form of delivery for an FH screening programme; we would like to highlight that NHS Health Check is an England service, and that it is aimed at an age range for which FH screening would be too late for significant health advantage. We therefore do not believe NHS Health Check is a useful initiative to discuss in relation to FH screening in the UK.

Support from individuals and families

We work closely with individuals and families affected by FH who live in south Wales.
Here, they have added their support to our consultation response.

> I support a UK National Screening Committee recommendation for a cascade screening programme for FH.
> Theo Coliandris, Cardiff; member of the FH Wales Steering Group; diagnosed with FH

> I support a cascade screening programme to find and diagnose people who have FH. I believe this programme could not only save lives, but also the cost to the health service providers treating people who have not been diagnosed (no symptoms).

> I feel a screening programme is a must.
> Anthony Davies; diagnosed with FH in 2005

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Reply from Dr Mackie

Thank you Nick, for your comments.

I have covered adults only because that it what Steve did in his review for me. I will need subsequently to look at children. I take your (and many other stakeholders) point about the NHS Health Check and have removed it as part of the document.

Anne