UK NATIONAL SCREENING COMMITTEE

Carrier screening for Spinal Muscular Atrophy

21 November 2013

Purpose

This paper provides background on the agenda item addressing carrier screening for spinal muscular atrophy.

Current policy

This is the first time the UK NSC has considered screening for this condition. The Committee was asked to review the evidence for screening by the Deputy Prime Minister following discussion with a constituent.

Current review

The review was undertaken by Sally Cartwright and aims to focus on carrier screening in the general population. The recommendation is that screening should not be offered. A number of criteria were identified for which there was a lack of evidence. For example

- a clear test cut off value was not identified and some mutation groups would not be identified,
- there is an uncertain genotype / phenotype association which would impact on the assessment of risk in screen detected carrier couples,
- there is limited information on the acceptability of screening in both health professionals and the public,
- no large trials have been conducted,
- the papers reviewed suggest that screening is unlikely to be cost effective.

Consultation

A consultation was held between 3rd May and 3rd August 2013. The following organisations were contacted British Society for Human Genetics, The Jennifer Trust for SMA, Muscular Dystrophy Campaign, Royal College of Paediatrics and Child Health, SMA Trust, SmashSMA.

Responses were received from The Jennifer Trust for SMA (incorporating the view of a parent of an affected child), Muscular Dystrophy Campaign, Royal College of Paediatrics and Child Health, SMA Trust, SmashSMA, Dr Felicity Boardman.

The majority of respondents were content with the conclusion of the review.

The most sustained commentaries were submitted by The Jennifer Trust and Dr Felicity Boardman. Both commentaries highlight criticisms of the document, in particular a lack of clarity on the context of screening (general adult population, antenatal or newborn). As a consequence both consider there to be insufficient of exploration of the specific issues related to the different contexts.

Nevertheless, there is much in these commentaries which helps strengthen the conclusion of the review. For example there is concern that the document does not:

- highlight the lack of UK data on the epidemiology for which there is a pressing need prior to the introduction of screening or the inability of the test to distinguish between types of SMA,
- sufficiently discuss the uncertainties and debates regarding the classification of SMA and the range of genotype / phenoptype associations,
- emphasise the lack of evidence or the complexities relating to the psychosocial implications of screen detected carrier status and the acceptability of screening in different populations.

Proposal

The following policy position is proposed:

Carrier screening for spinal muscular atrophy in the general adult and pregnant populations is not recommended.

There is insufficient information on the epidemiology, the acceptability of screening and on the psychosocial implications of screen detected carrier status. There are concerns that the test is unable to reliably distinguish between types of SMA and about the way in which the range of genotype / phenotype associations would affect counselling and reproductive decision making.

Action

The UK NSC is asked to consider the above.

UK National Screening Committee
Spinal Muscular Atrophy - an evidence review

Consultation comments

Below you will find the comments for the Spinal Muscular Atrophy evidence review.

Organisation:	The SMA Trust		
Name:	V. Christie-Brown, Research Co-ordinator	**Email address:**	[redacted]

Section and / or page number	**Text or issue to which comments relate**	**Comment** *Please use a new row for each comment and add extra rows as required.*
N/A		After careful consideration of the evaluation of carrier screening and a specific meeting with the Chair of our Scientific and Clinical Advisory Group on this issue, the SMA Trust supports the conclusions drawn from the UK National Screening Committee's evidence review. However, we understand that larger trials need to be conducted. If such larger studies were to be carried out, the SMA Trust would be very interested in being involved.

A comment from [redacted]:

The SMA consultation came about as a result of our presentation to Nick Clegg and Norman Lamb at the House of Commons last year.

We were invited to give details about our daughter [redacted] and our SMASHSMA campaign.

This was done at a reception hosted by Nick Clegg.

We were told at the time that as stakeholders we would be

- Contacted by Mr Lamb following the presentation - this never happened
- Invited to take part in the consultation - this never happened
- Kept up to date with the consultation - this never happened

The SMA consultation is the best kept secret in the world. Despite having 44,000 twitter followers and spending a great deal of time highlighting SMA and seeking screening we were not told that the consultation had started.

We have decided that as the consultation is closing shortly we do not wish to submit any further evidence or key points. We have been treated badly and hold no confidence in the enquiry or its findings.

The link below is our only submission to your enquiry

http://www.youtube.com/watch?v=34RmmLWhr80

It tells the tale of a little girl who died from SMA - and highlights the points we tried to make the government aware of .

The fact that we were not contacted is shameless.

[redacted]

My personal email is [redacted]

Muscular Dystrophy Campaign response to the National Screening Committee's Policy on Screening for SMA
August 5th 2013

The Muscular Dystrophy Campaign welcomes this evaluation of a national carrier screening programme for spinal muscular atrophy. There are, however, some points to which further consideration should be given.

Section 5.4
The analysis of the possible cost effectiveness of a national carrier screening programme was based on two studies which modelling the potential cost effectiveness of such a programme. As the evaluation states, the first study used a sensitivity lower than estimates suggested in other studies to model cost effectiveness. Increasing sensitivity could reduce the number of cases of spinal muscular atrophy and the cost of care associated with those cases. This could make the test more cost effective than the model suggested.
The second study that modelled cost effectiveness was a poster presented during 2009. As such, the work was not peer-reviewed and has not been published in a peer-reviewed format since. We therefore feel that this study should not be used to assess cost effectiveness.
Even if both studies take into account the cost of medical care (as the evaluation says, it is not clear in the second study), they did not consider the costs beyond medical care.
Many patients and their families living with spinal muscular atrophy face extreme financial hardship due to the additional costs associated with caring for those with this rare condition. As a result of providing care and support for their children, partners or relations, people are often unable to work. Families must adapt houses, schools must provide specialist support, and the government provides benefits.

Taking these costs into account alongside those of medical care would undoubtedly increase the cost effectiveness of any screening program.

Section 6
The evaluation cites the lack of information for parent education as a reason for not recommending the introduction of a screening programme. This should not be considered when assessing whether a programme should be introduced.
With no testing programme in place, there is clearly no requirement to produce this material, so the request that the material be in place before a programme is considered should be re-examined. If an effective test which meets all the other requirements was available, we believe that educational material should be produced to support the introduction of that test.

About the Muscular Dystrophy Campaign

The Muscular Dystrophy Campaign is the leading UK charity fighting muscle-wasting conditions. We are dedicated to beating muscular dystrophy and related neuromuscular conditions by finding treatments and cures and to improving the lives of everyone affected by them.

Our work has five main focuses:

- We fund world-class research to find effective treatments and cures
- We provide practical information, advice and emotional support for individuals with muscle-wasting conditions, their carers and families

- We campaign to bring about change and raise awareness of muscular dystrophy and related neuromuscular conditions
- We award grants towards the cost of specialist equipment, such as powered wheelchairs
- We provide specialist education and development for health professionals.

Organisation:	Royal College of Paediatrics and Child Health		
Name:	Comments submitted by RCPCH, with thanks to the following for commenting: • Dr John Gibbs (response on behalf of SG Secretary, British Academy of Childhood Disability)	**Email address:**	[redacted]

Section and / or page number	**Text or issue to which comments relate**	**Comment** *Please use a new row for each comment and add extra rows as required.*
Page 22	Conclusion	Members of BACD agree that population screening for carriers of spinal muscular atrophy would NOT be justified at the present time (for the reasons given in the conclusion on pages 22 and 23).

Jennifer Trust Screening Consultation submission
(as well as the comments form there are two attachments)

Organisation:	The Jennifer Trust for Spinal Muscular Atrophy		
Name:	Liz Ryburn Support Services Manager	**Email address:**	[redacted]

Section and / or page number	**Text or issue to which comments relate**	**Comment**
Intro 1.	This paper reviews the evidence for a carrier screening programme for SMA in the general population in England.	There seems to be some confusion throughout the paper regarding the **timing and the target group** for carrier testing. Though the conclusion refers to a **population-wide carrier screening programme**, the title of the paper and the source material referred to covers a wide range of testing. It is not always clear whether the author is referring to pre-conception testing or testing in early pregnancy. Different terms are used. (e.g. 3.3 pg. 12 refers to pre-natal testing). There is also reference to general screening tests; tests on people already known to be carriers and use of the term carrier screening. Is this screening of people known to carry the disease or screening for potential carriers? It is not always clear and tests applicable to both possibilities are discussed. Consistency of terminology would be helpful, e.g. “carrier testing before conception or in early pregnancy” was cited in one article and “pre-natal screening” in the other. A glossary of terms would also be helpful. We know it is a very complex area. , Our Support Services staff, with a level of familiarity with the area, had to read this paper several times to understand the evidence. Greater clarity would make this paper more accessible to the general public and to carriers of SMA who are

		personally grappling with and debating these issues. We communicated the screening consultation to our readership via our website and e-news inviting them to advise us of their views. Only one person made contact (attached) .
2.2 page 5 and 6	The Epidemiology and natural history of the condition	This is understood (summary pg. 5 gives a description) and varies greatly according to the Type of SMA. We are concerned that the studies referred to on pg. 6 are quite old and may not reflect the advances in management options for SMA (e.g. Standards of Care for Spinal Muscular Atrophy) over the last 10 years in the UK. We also note that they are US studies where the management of SMA differs from UK practice – notably in the US invasive procedures such as gastrostomy tube placement and invasive ventilation i.e. tracheostomy, are undertaken more commonly on children with SMA Type 1 in the US which might account for the statistic of 30% surviving to 20years. This is not applicable to the UK where almost all babies do not survive past their 2nd birthday. We note also that the focus in these studies is SMA Type 1 and 2 only. There is no mention of SMA Type 3 and Adult Onset. **One very big issue with all tests is their inability to discriminate reliably between the types of SMA**. In general couples with a history of SMA would have children with the same type of SMA but this is not always the case. **It is not possible for the type of SMA to be determined / predicted for couples with no history of SMA.** We suggest that the paper should make this observation much more explicit
2.4 page 9	**If the carriers of a mutation are identified as a result of screening, the natural history of people with this status should be understood.** No papers were found in this review regarding natural history or *psychosocial implications of carrier status.*	The following psychosocial studies are available: Dr Felicity Boardman's PhD thesis: '**The Role of Experiential Knowledge in the Reproductive Decision Making of Families Genetically at Risk: The Case of Spinal**

		Muscular Atrophy' http://wrap.warwick.ac.uk/4510/1/WRAP_THESIS_Boardman_2010.pdf **Boardman, F.** 2014. Knowledge is Power? The Role of Experiential Knowledge in Genetically 'Risky' Reproductive Decisions Sociology of Health and Illness 36 (3) (in press). Available at: http://wrap.warwick.ac.uk/52313/ **Boardman, F.** 2011. 'Negotiating Discourses of Maternal Responsibility, Disability and Reprogenetics' in Lewiecki-Wilson, C. and J. Cellio (eds) Disability and Mothering: Liminal Spaces of Embodied Knowledge Syracuse University Press. The top one focuses on the ethical and social dilemmas faced by people from families living with SMA facing reproductive decisions, the second one, the book chapter, focuses on the dilemmas faced specifically by women with SMA and their decisions around reproduction. Both publications are from Dr Boardman's PhD research. Many studies around reproductive decision making and genetics focus on able bodied parents with disabled children but women with SMA face very particular issues and dilemmas when considering having children. This chapter details some of the dilemmas they described in Dr Boardman's interviews with them. Dr Boardman is also being funded and has received ethics approval to proceed with her further SMA related study: **BSREC Ref: Selecting futures: the Social and Ethical Implications of Genetic Screening. REGO 2013 – 282'** Another paper that might be relevant (which itself refers to other

		studies) is: **Imagined futures: how experiential knowledge of disability affects parents' decision making about fetal abnormality** France, E. F., et al. *Health Expect 2012; 15 (2): 139-156* BACKGROUND: Knowledge of disability is considered key information to enable informed antenatal screening decisions by expectant parents. However, little is known about the role of experiential knowledge of disability in decisions to terminate or continue with a pregnancy diagnosed with a fetal abnormality. OBJECTIVE: To explore the role that expectant parents' experiential knowledge of disabilities and conditions can play in real-life decisions to continue or end a pregnancy with a fetal abnormality. DESIGN: Secondary analysis of qualitative narrative interview data informed by contextual systems framework. SETTING: Participants were recruited throughout the United Kingdom and interviewed between 2004 and 2006. PARTICIPANTS: Twenty-four women and four of their male partners who had direct or indirect experience of disability or illness and who had proceeded with or ended a pregnancy diagnosed with a fetal abnormality. FINDINGS: Most respondents recounted using their experiential knowledge of disability, whether of their unborn baby's condition or of a different condition, to try to imagine the future for their unborn child, themselves and their family when making their decision. Some, who were considering continuing their pregnancy and had little or no experience of their unborn baby's specific disability, sought out others' experiences of the condition following antenatal diagnosis. The nature of a parent's experiential knowledge did not predict whether they continued with or terminated their pregnancy.

		DISCUSSION: Prospective parents may find it helpful to discuss their existing knowledge of their unborn baby's condition with health professionals who are aware of the influence this might have on parents' decisions. **http://www.ncbi.nlm.nih.gov/pubmed/21624022**
3.1 Pg. 9	**There should be a simple, safe, precise and validated screening test**	There is some information on false positives within the text, i.e. percentage chance and how this can happen. However, tests are currently unable to reliably determine the type of SMA that would potentially develop because there is not a perfect correlation between SMN2 copy number and disease severity. It must be remembered that the classification that has been determined for SMA is a man-made construct that helps to determine prognosis, and is not infallible. There are a number of reasons why patients may fit one criteria and not another. Although the 'Types' are agreed and recognised, the severity of SMA lies on a continuum, so there will always be borderline cases.
Section 3.3 page 13	"A further study on the American population…" acceptance rates for carrier testing	It would be important to know what information and education programme was used that was a basis for decision making (see next point). This is not mentioned. Decision making in the US may be very different from decision making in the UK and may be influenced by factors such as: • The cost of medical care and specialist equipment during the life of a severely disabled child under a US private health care system versus the UK NHS health and social care service system • The difference in management options for SMA Type 1 (more children receiving invasive ventilation and gastrostomy in the US) Decision making about genetic testing in Israel is also very different from US and UK.
3.3 – 3.4 Pg. 12 - 13	The test should be acceptable to the population. There should be an agreed policy for further diagnostic investigation of individuals with a positive test result and the choices available to	The possibility that the person undergoing carrier screening could themselves having a late onset form of SMA and the impact of this information is largely not covered in the report. These individuals could be asymptomatic or mildly symptomatic at the time of any test. The

	those individuals	ethical implications of discovering a diagnosis of SMA if the individual were also pregnant and communicating this information to them would need to be carefully considered. If screening for SMA was introduced for newborns and the type could be established as adult onset, serious consideration would need to be given as to whether or not it is ethical to inform parents of this. Further research is needed for all these possibilities.
Pg. 13.	There is a need to ensure couples are adequately educated…..	**This is very important**. Given it is not possible to predict the type of SMA for parents who are found to be carriers and have no family history, it would be extremely difficult to offer both pre-conceptual counselling and appropriate post result information as to what life could be like for any child they have with SMA. The Utah education program for example http://learn.genetics.utah.edu/sma/ focuses on children with SMA Type 1 and gives less information about children and adults living with SMA Type 2 and Type 3 or Adult Onset SMA which are the other possibilities.
3.4 Pg. 13.	'Before 1995, linkage analysis…'	Only SMA Type 1 is mentioned with reference to this. We wondered why.
3.4 Pg. 13.	Methods for prenatal testing … maternal blood'	We were not aware that this is in use in the UK for SMA (We understand that Heather Skirton, Professor of Applied Health Genetics, Plymouth University is currently undertaking a study into parental carrier status testing and testing in pregnancy "The study is looking at a new test that is **being developed which may in the future** be offered to women during pregnancy who are at an increased risk of having children affected by certain genetic conditions including spinal muscular atrophy, thalassaemia and cystic fibrosis."
Pg. 14	'A further limitation is that it is not possible to inform two carriers of the SMA type their offspring is likely to have.'	As mentioned elsewhere we believe this needs far greater emphasis in the paper.

Pg. 15	'In one prospective cohort study, genetic counselling…3 stages'	This paragraph shows the level of genetic counselling that would be required. This would have enormous practical and cost implications
Pg. 19 Para 5.	One study… found many respondents to report negative experience with genetic counselling possibly because it occurred at the time of diagnosis or shortly after which is a difficult period emotionally."	We agree that parents may find this difficult in this situation however, if the counselling isn't discussed / offered at this time it may not be easy to find another suitable opportunity until they find they are facing another pregnancy.
5.4 Pg. 20	Opportunity costs	These are US studies where health and social care systems and cost implications differ greatly from the UK.
6. Pg. 22	Conclusions: Would not be cost effective	The numbers quoted are quite telling in that based on a purely financial analysis, it is not viable to indiscriminately test for SMA. However, the cost of screening will almost certainly decrease in the future due to improved and reduced costs of testing. More large-scale UK research into this needs to be conducted before blanket screening can be advocated.
	Conclusion: There are limitations to the screening test currently available	We are mindful of the following points: • Screening tests currently in use for other conditions are not 100% accurate, and there will always be cause for doubt. With genetics there is very rarely 100% certainty in anything. • Carrier screening can be seen as devaluing disabled people living with a condition – in this case people living with SMA Type 2, 3 and Adult Onset. • Many parents who have had and lost babies to SMA Type 1 feel very strongly that no other parent should have to face this possibility and that population wide carrier screening should be available • **Tests are currently unable to ascertain the type of SMA – in particular for prospective parents with no family history. This is the most telling limitation.**

	Conclusion: A very considered and consistent approach to patient education and genetic counselling	We agree this would be critical. It would need a significant investment in terms of content and personnel. There would need to be extensive consultation with the SMA community. We suggest that Dr Boardman's studies will be very pertinent to this.
	Conclusion: There is ltd evidence from pilot studies and no larger trials	We agree that this needs to be addressed.
	Conclusion: Limited information on the acceptability of a programme to health professional and to the public	We imagine that this consultation will result in some response from health professionals. We feel strongly that there should be more consultation with people who are living with, and who have been affected by, SMA. We suggest that Dr Boardman's studies will be very pertinent to this. We agree there should be public consultation. For this there needs to be a much simpler accessible summary of the issues. We suggest this should be consulted and agreed with representatives of the SMA community.

Attachment 1

View of Parent of a baby with SMA Type 1

I could not imagine having to go through again, what my partner and I went through when our daughter was diagnosed with SMA type 1b and subsequently died of the condition in [redacted] at just 18 months old .

There are thousands of people walking around the UK who are carriers of SMA and they have never even heard of the condition.
Although I would never be without the special time we had with our beautiful girl I also would not put myself, my family or a baby through the heart ache and pain of dealing with such a cruel genetic condition.

Like Downs syndrome if SMA carrier testing was done on mums to be in the early days of pregnancy they could make an informed choice about continuing with the pregnancy or making the difficult decision to terminate if the baby was found to have SMA. At least this way they are informed . Been told your baby has a life limiting condition is truly devastating and I would not wish it on anyone.

Every woman in the UK has the option of having their pregnancy tested for some chromosome abnormalities some that cause significant disabilities and health conditions however non are as severe as SMA which is the UK biggest genetic killer of under 2's. So why prenatal testing so readily available for those and not for SMA?

Carrier testing would be a stepping stone for parents, if they were found not to be a carrier then great things carry on as normal. However, if parents are found to be carriers at least something can be done and options explored.

Been given a diagnosis of SMA is a death sentence to a baby and so difficult to deal with. Carrier testing would help parents to make informed decisions and not have to go through the pain that unfortunately [redacted] and I and many parents of SMA babies have had to go through.

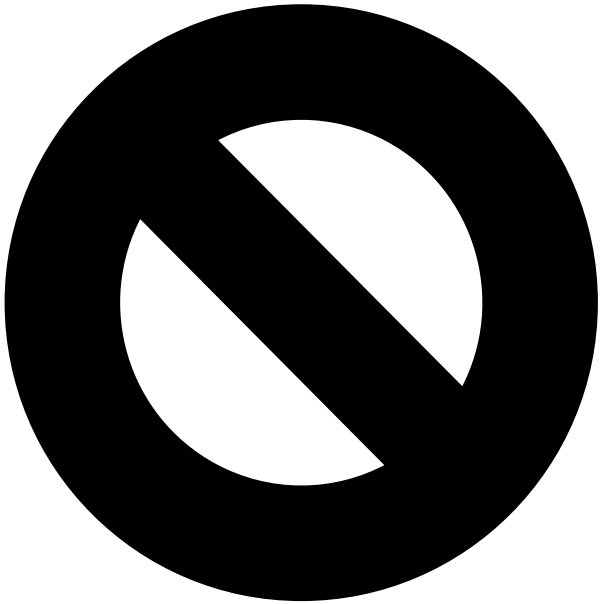
Attachment 2

View of Parent (who is also a doctor) of a child with SMA Type 2

Some time ago now - it was actually October last year- and in response to a letter to no.10, I received a reply from a man responsible for "Ministerial Correspondence and Public Enquiries" at the Department of Health. It told me that the National Screening Committee was currently reviewing the evidence for SMA screening against its criteria and that a public consultation would commence shortly.

Some eight months on, despite knowing that the process of SMA screening was about to be taken seriously and a consultation was on the cards, there had been no indication that it was going on; no transparency, no letters or emails from the charities working in partnership with the NSC through the consultation, no direct communication with those who have lost babies to this terrible genetic killer nor with those living with the reality of SMA in the day to day. Surely these people should be given the chance to have a say? To have their stories heard? These stories, collectively hold a power so infinite and unquestionable that every person affected by SMA should have been informed of the process being undertaken. Those affected, parents of children with SMA, family members and friends should be able to read the document and understand what is being said - or at least an information leaflet, easy to follow, clear and concise and aimed at an appropriate reading age - so that they can respond. Instead the process seems somewhat clandestine, aimed at professional people who are "in the know", who have an understanding of the screening process, of science and statistics and confidence intervals, and these are the very people who are - more than likely - living lives unaffected by SMA.

So here I am - having coincidentally stumbled across a post on The Jennifer Trust - a mummy to a beautiful little girl who happens to have SMA, living an unfamiliar life with a disabled child and managing somehow to make it wonderful, wanting to tell you, the people who will make a decision about the future of a screening programme, exactly what I think about screening for SMA.



Xxxxx at 8 weeks - long before SMA came into our lives. The day we were told that our daughter Xxxxx had SMA 2 was the worst day of my life, my world ended in that moment, all hope was lost and our future was unwritten. The disbelief, the anger, the sadness, the grief were immense and overwhelming, but I had to get up each and every day thereafter to greet the day and care for my family. Xxxxx was blissfully unaware and with innocence on her side, she kept me going. She was the reason to get up in the morning. Her smiles made my days. Her joy and exuberance flowed through the house and for that, at least, I was grateful. For a while she remained Xxxxx; for all intents and purposes to those who didn't know her diagnosis, unaffected by SMA. But then came her Panthera Micro as her peers began to walk; her standing frame to help her bones grow strong and to keep her muscles long and straight; Snappie as her friends started to explore the beautiful world around them, hopping, skipping and jumping; adaptations to our house and discussions with social work and occupational therapists about costs, funding and responsibilities; a WAV to transport Snappie and all the goods and chattels needed; a car seat to keep her safe at any cost; more adaptations and tracking hoists to enable us to have time as a couple, to allow others to care for her. For many carers, SMA and disability become all consuming with sleep deprivation being common, low mood and depression a possibility, and the need to alter working hours or indeed become a full-time carer a reality.

What about Xxxxx? Well, she was and still is Xxxxx. No more. No less. She is cheeky and headstrong and independent in her own way. She loves singing and painting, cake and ice cream, asking questions and never taking no as an answer.

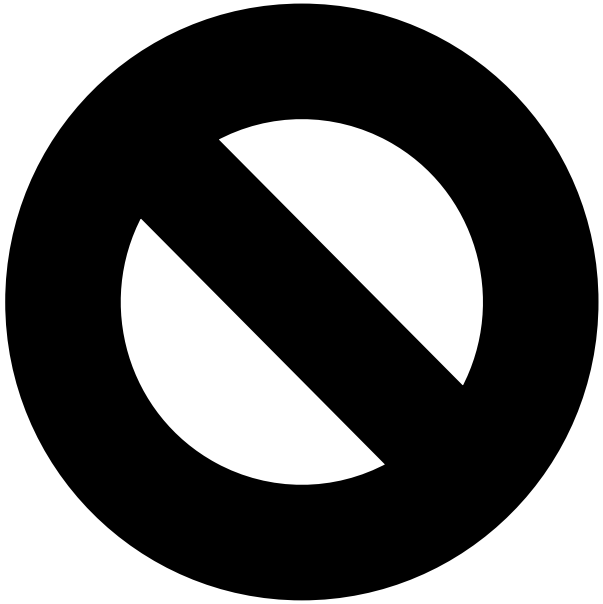
She knows no different - her life is inexplicably bound to SMA and I love her no less because of it. I will do anything and **everything** for her and for my family.

She brings so much joy to me, to my family and to those around her; she keeps me going.
But do I wish that she didn't have SMA?
Yes.
Do I wish that I could have been screened before my pregnancy to see if I was a carrier for SMA?
Yes... most definitely, yes!

I would have been screened to save myself and my husband from the pain of having our hearts broken in two at the point of her diagnosis.

I would have spared my family and my friends the heartbreak of seeing our hopes and dreams shatter before their eyes.
I wouldn't now covet a normal family life in which we didn't need to consider accessibility and transport and adaptations and grants and acceptance and support and respite; a family life in which every day didn't feel so much like a battle.
I would not have to worry that a sniffle and a cough would turn into something more serious that would mean hospital admission and ventilation and prayers for her to be spared, prayers that she would see a life of three scores and ten.

I would be living the life I dreamt of before SMA came into my life.



These are, however, my worries and concerns and thoughts; selfish but honest as they are, I do not know what Xxxxx feels about SMA and disability, nor whether she would advocate a screening programme and I cannot as a result speak for her - she is only 4 after all. Some say SMA is a good disability to have, the muscle weakness being more than balanced by an above average intelligence, and that the world is their oyster. I still wish that I had had a choice and that is what this screening programme comes down to: should women contemplating pregnancy have the choice of living with a child with disability, with all its ups and downs, just as they do with so many other genetic conditions both ante-natally and after birth? Would you want to have that choice? I certainly would.

This is Xxxxx recently: sma 2 in all its glory - beautiful and yet totally dependent

To Whom It May Concern: UK National Screening Committee (UK NSC),

I understand what you do. I do understand.

You advise the government and the NHS about all aspects of screening. You look for research evidence and assesses this evidence against a criteria which looks at the condition, the test, the treatment and how effective and acceptable the screening programme is. You also evaluates the cost of the programme with the ultimate goal of ensuring that the programme does more good than harm and at a reasonable cost.

As a Doctor of Medicine, I understand better than most the evidence, the criteria, the effectiveness and acceptability of a screening programme. I can read your expert's opinion, even marking the time spent reading the report as continuing professional development because I can learn from it, reflect, change my practice and teach from it.

The salient points that I take from the report are as follows:

You advise the NHS of the four countries of the UK and therefore your paper should be looking at the evidence for a carrier screening programme for SMA in the UK and not just in England.

SMA is the second most fatal autosomal recessive disease (after cystic fibrosis) and yet few people, and that includes health care professionals, outwith the SMA community know anything about this disease but know much more about CF.

Carrier prevalence estimates are between 1 in 76 and 1 in 111, lower than the 1 in 40-50 I expected.

The clinical progress of SMA is highly variable but with many complications possible, SMA has a significant impact of the quality of life of the child and their family, but also on the NHS and society too.

Overall survival is improving which is wonderful but at the same time this means an increasing burden of care - emotional, physical, financial - on the family and on society.

The genetics of SMA are now better understood, however they are complex and limitations exist when applied to carrier testing. It is also impossible to determine the type of SMA a couple deemed carriers may have, so counselling them with regards to the quality of life and prognosis for their child would be impossible.

There is no treatment or cure for SMA although research is ongoing, specifically in the area of managing the severity of disease, with treatment potentially being possible during the early course of the disease - this in itself, however, suggests that pre-natal or at least ante-natal testing would be necessary if such a therapy comes to fruition.

There is no evidence of sufficient hierarchy to support that a screening programme for SMA would reduce mortality or morbidity.

That you have not taken into account any of Dr Felicity Boardman's work on the psychological impact of carrier screening seems to be rather a large oversight on your behalf.

This review should not have been aimed at ante-natal carrier screening (CVS or amniocentesis) but at women contemplating pregnancy who, through the improved education and subsequent awareness of the general public about SMA, should be allowed to make an informed decision regarding pre-natal screening of themselves and subsequently, if their status is positive, their partner.

The conclusion that I draw, that is screaming out from within the lines of the report, obvious to me and probably to many others, is this:
At this time a screening programme for SMA is not recommended, however, increasing the public's knowledge and awareness of this genetic disease is paramount, enabling further resources to be made available and directed towards the research of the complex genetics of SMA; the development and implementation of a sensitive and specific carrier genetic screening test; and the advancement of an evidence-based effective treatment.

A pre-natal screening programme should be considered in light of ongoing research into treatment which can manage the severity of disease (and, perhaps slow the progress of disease?) so as to not discriminate those with the more severe forms of SMA, allowing treatment to begin early.

The burden of SMA - physical, psychological, and financial - on individuals, families, communities and society should also be considered when evaluating the cost-effectiveness of screening: to do this a period of transparent public consultation must be considered.

To finish; I understand what you do, UK NSC. I understand the conclusions that you draw. I understand as a Doctor, but I also understand as a mother to a child who has SMA 2 and this is the bottom line:

The SMA community needs a louder, more dominant public voice; we need to be heard. We need to increase the public's understanding of what SMA is and how it affects lives. And above all we need more money and resources injected into the research of the genetics and treatment of SMA.

Kind Regards
A doctor and a mummy

Organisation:	Warwick Medical School		
Name:	Dr Felicity Boardman	**Email address:**	[redacted]

Section and / or page number	**Text or issue to which comments relate**	**Comment** *Please use a new row for each comment and add extra rows as required.*
p. 4 and p. 7	Carrier frequency in general population	It appears problematic that there is significant variation in estimations of carrier frequency between different studies as well as between ethnic groups. More evidence is needed to determine the carrier frequency specifically in the UK population, as only one UK study is cited, in order to both justify the need for a screening programme as well as informing the general population. We are also not provided with the number of births affected by SMA in the UK within this report- I therefore think more UK-specific data is needed. The possibility of different carrier frequencies existing between ethnic groups further underlines the need for UK-specific data.
p. 8	The Genetics	The genetics of SMA is complicated meaning that testing for it always carries the risk of incorrect results because of the techniques used and the variations in individual genetic make-up, for an example see Thauvin-Robinet et al. (2012).
p.5 p.7&8	The types of SMA and genetics	There is considerable debate within the medical community as to how SMA should be classified, and also whether the diagnosis can be made upon genotype or phenotype presentations, with debates also on-going concerning the number of different 'Types' that can be identified (Russman, 2007). As Opera et al. (2008) discovered when comparing siblings within families that had the same deletions/mutations in SMN1 and the same number of SMN2 genes, there was a wide variety of phenotype presentations and some individuals did not develop SMA at all. The researchers suggest that this could be to do with a protein called Plastin 3 which appeared to ameliorate disease severity. They argue that there are probably a large number of genes within our genome that act to modify SMA severity, therefore undermining the argument that disease severity can be determined by SMN2 copy number (Opera et al., 2008). Indeed, in my interview study with families living with SMA (Boardman, 2010), there were several participants who did not fit the typical pattern of 'typing' and many participants reported that they found the categorisations unhelpful and uncorrelated with the way in which they actually experienced SMA. Within my relatively small sample (64 participants) there were also four families within

		which siblings were diagnosed with different types of SMA, which may further highlight the lack of precise genotype/phenotype correlation, but also the imprecision of the typing of SMA. Some parents of children diagnosed with Type I SMA reported that they experienced the typing of SMA as an 'alienating' experience as they felt they had to 'explain' to other parents of Type I children why their child had survived when the expected trajectory is infantile death. The typing of SMA may therefore be regarded as overly simplistic and not always useful for families living with SMA.
p.6	Quality of life	Quality of life for adults living with SMA emerged from my study (Boardman, 2010) as a complicated phenomenon not linked to disease severity in any straightforward way. Indeed, those diagnosed with the (clinically) more severe Types of SMA (I and II) often reported more positive life experiences than those diagnosed with Type III, and particularly by those adults whose level of impairment/disability had remained stable since childhood. The most negative experiences were reported by those participants who experienced marked deterioration in their SMA symptoms over time, irrespective of the resulting level of impairment and disability. Type III SMA is commonly associated with gradual deterioration over time, which requires considerable adjustment to new identities and abilities, e.g. wheelchair use/walking aids. Medical classifications of SMA alone may therefore not provide a full picture of the resultant quality of life associated with SMA across the spectrum of severities as the lived reality is mediated by a range of factors, including social and environmental aspects, as well as psychological resilience.
p.9	Psychosocial implications of carrier status	There is a general lack of evidence surrounding the psychosocial implications specifically of carrier status in relation to SMA. My research (Boardman, 2010) found that many relatives of the person diagnosed with SMA opted to forgo carrier testing on account of the increased anxiety the information could induce. Direct experience of SMA in the family often mediated how family members felt about undergoing carrier testing- some were more certain that they wanted to prevent further lives being affected by SMA, others felt that they had witnessed their family member live successfully with SMA and thus they opted to forgo testing as they did not regard SMA as a condition for which they would terminate a pregnancy (given that there is no treatment) and some participants reported feeling trapped between wanting to prevent the recurrence of SMA but also wanting to validate the quality of their family member's life by refusing testing

		(Boardman, 2014). It is not known how the general population, with no prior experience with SMA, would react to their carrier status, however this is an important consideration and evidence is needed. It is noteworthy that 41.6% of those offered free carrier screening in Prior et al.'s (2010) study refused. 27.3% of these test refusers stated that they simply did not wish to know their carrier status and 13% stated that knowing their carrier status would increase their anxiety (p. 1613). The numbers of those refusing carrier screening in this study appears high given that the research was conducted with a 'motivated' sample population already undergoing genetic counselling. 'Increased anxiety' was also cited as a reason to refuse carrier screening by one participant in a study of the acceptability of screening for SMA by Ohio State University (Rothwell et al., 2013). Further evidence is needed regarding the pyschosocial implications of carrier status on the general population in the UK.
p. 11	The test	The possibility that the person undergoing carrier screening could actually be identified as having a late onset form of SMA themselves is largely overlooked in the report. These individuals could be asymptomatic or mildly symptomatic at the time of screening, but gene dosage analysis would identify them as having a late-onset form of SMA. Indeed, Su et al.'s (2011) prospective cohort study in which 107, 611 pregnant women were screened for SMA, identified four pregnant women with no copies of SMN1, indicating that they had SMA themselves. These women had mild symptoms of muscle weakness but attributed it to other causes (e.g. falls in childhood) and did not know that they had SMA until they underwent screening. The ethical implications of discovering a diagnosis of SMA in the would-be parent and communicating this information to them during this critical and sensitive point of pregnancy needs to be carefully considered. Further research is needed to explore the views of individuals with adult-onset forms of SMA, as well as individuals from the general population, regarding their attitudes towards carrier screening for SMA, and the implications of a diagnosis at this point, particularly for pre-symptomatic individuals. Moreover, the possibility, and implications of, a misdiagnosis in the pregnant woman at the point of screening, due to the limitations of the test (e.g. some individuals with no copies of SMN1 do not develop SMA at all- Opera et al., 2008) need to be carefully considered. If screening for SMA was introduced for newborns, serious consideration would also need to be given to whether it is ethical to inform parents that their child will

		develop an adult-onset condition. A study conducted by Meldrum et al. (2007) found that 77% of the parents that they surveyed with a child with SMA were in support of newborn screening if the test identified SMA 10 years before the onset of symptoms, and 92% were in support if the screening test identified SMA 6 months before symptoms onset. However, the sample size for this study was small (n=103) and participants were not asked about attitudes to newborn screening if there is a delay of >10 years before onset of symptoms, which is perhaps a more realistic time lapse to symptoms for late onset forms of SMA (e.g. Type IV), suggesting that further research is needed to explore the social and ethical implications of diagnosing a newborn with an untreatable, and adult-onset condition.
p.12-13	The test should be acceptable to the population	There are limited studies on the acceptability of SMA carrier screening for the general population, however those that have been carried out in the USA report relatively high levels of test refusals – e.g. 41.6% of Prior et al.'s study sample refused a free of charge SMA carrier screen (2010). The main reasons for refusing screening, as reported by test refusers, were: lack of concern about SMA, a belief that a positive test result would not change pregnancy management, not wanting to know genetic status and increased anxiety (Prior et al., 2010). The odds of agreeing to screening were 79% lower among African Americans than among Caucasians, suggesting that perceptions of the test are linked with cultural, ethnic and religious backgrounds. Although Cartwright states on page 13 that a study in Israel found a demand for SMA screening (Ben-Shachar et al., 2011), a more recent study conducted in Israel since SMA screening has been introduced found that compliance with SMA screening within the Arab population was very low (Sukenik-Halevy et al., 2012). Only 20% of their study sample (n= 167) accepted the screening (Sukenik-Halevy et al., 2012). The authors attribute this to the fact that payment is required for SMA screening in Israel (unlike Cystic Fibrosis screening which is provided free of charge), and further research may be called for following the introduction of free SMA carrier screening in March 2013 (Israeli Ministry of Health, 2013). The studies exploring the acceptability of screening, moreover, have only been undertaken in America and Israel, two countries where genetic screening is far more widely available than in the UK. The acceptability of the test in the UK

		population is unknown and generalisations from existing studies do not necessarily translate in the UK context where fewer conditions are screened for and a contrasting system of health and social care provision exists. Whilst studies of the acceptability of screening exist, questions also emerge as to the reliability of the reported data. A recent US study in the states of Utah and Colorado (where newborns are screened for 30 conditions using an opt-out approach) found that most participants (from their sample of 70 parents) were comfortable with newborn screening for SMA (Rothwell et al., 2013). However, this study contains many inherent biases- the researchers made their own favourable opinions towards the development of an opt-out approach for screening for SMA known at the start of their focus groups with parents, which may have influenced the views of the participants. Moreover, their educational material, in the form of a video about SMA shown to participants prior to their focus groups (available online at: http://learn.genetics.utah.edu/sma/), presented SMA as a condition of childhood- no adults were featured. Furthermore, the emphasis within the educational video was on the possibility of therapies and interventions being implemented at an earlier time point as a result of newborn screening for SMA. However, these references to early therapeutic interventions could perhaps be interpreted as misleading when presented to a population unfamiliar with SMA given that there are currently no effective treatments available, and interventions for affected infants focus on symptom management rather than cure. Moreover, it is unclear from the literature whether *earlier* interventions have a significant impact on outcomes for babies diagnosed with Type I SMA nor the acceptability to parents of pre-symptomatic interventions for these children. In line with the ACOG's recommendation, high quality educational materials need to be developed around SMA. Indeed, the educational materials used for the participants in Prior's (2010) study of the acceptability of screening were developed by the Claire Altman Heine Foundation, an American pro-screening campaign group for SMA, which could have potentially introduced bias to the study, although the materials are not made available to the reader to make this assessment. As per the AMP's (Muralidharan et al., 2011) recommendations, families and individuals living with SMA (in all its forms) should be consulted, and involved in the implementation of any screening programme, including the development of educational materials around SMA. Indeed, the representation of SMA within

		these education materials is absolutely critical. However, there is a lack of research on the views of this population. Individuals diagnosed with the condition in question have often been under-represented in studies of the acceptability of screening programmes more generally, e.g. in relation to Cystic Fibrosis, only one person with CF was included in Watson et al.'s (1991) study on the acceptability of CF screening (0.1% of total sample), four individuals with Cystic Fibrosis (9% of total sample) were included in Poppelaars et al.'s (2003) study and 18 individuals with Cystic Fibrosis (12% of the sample) were included in Maxwell et al.'s study (2011). In spite of this under-representation, individuals living with SMA and their family members have a considerable contribution to make to the debates around the acceptability of screening, not only on account of their unparalleled expertise on the daily reality of living with SMA, but also because population screening may have particular consequences for this group in terms of welfare and support (Maxwell et al., 2011). My current ESRC funded project, 'Imagining Futures: The Social and Ethical Implications of Genetic Screening' will address this gap in the literature through one on one in-depth qualitative interviews with families living with SMA (n=40), as well as a nationwide survey of all families living with SMA who are registered with the Jennifer Trust for Spinal Muscular Atrophy (approx. 2,000 families and individuals). The interviews and survey will explore the families' attitudes towards newborn, pre-conception and prenatal genetic screening for SMA and analyse their conceptualisations of the ethical and social issues surrounding each one. The research is due to be completed in 2016. It is anticipated that this study will lead on to further work with the general population to explore public attitudes towards screening for SMA.
p. 14	There should be an agreed policy for further diagnostic investigation of individuals with a positive test result and the choices available to those individuals	Do we have estimates of the rates of false positives/ 'unnecessary terminations' in the literature? The point at the bottom of page 14 that it is not possible to inform two carriers of the SMA type in their offspring is a really key issue for a screening programme, as research has indicated that would-be parents have very different attitudes towards termination of pregnancies according to the perceived severity of the condition affecting the foetus, which may be different in contrasting cultural contexts (Alsulaiman et al., 2012). Given that SMA is so extremely variable (even within the Types), counselling associated with screening is highly problematic. There are various estimates as to the proportion of SMA diagnoses that fall into each of the Types (60-70% of SMAs are

		estimated to be Type I, 20-30% are Type II and 10-20% are Types III and IV) (Prior et al., 2008; Ogino et al., 2004) but UK data are lacking. In terms of the counselling of would-be parents undergoing screening for SMA, statistical data on the prevalence of the different Types of SMA is an inadequate basis for parents to evaluate their genetic risk, and high quality educational materials on SMA need to be produced. On page 15, the example of Su et al's (2011) study is given, but it is difficult to assess the quality of the brochures and information that were provided to the screened participants as we are not given access to copies by the researchers. However, the way in which SMA is presented within these documents is likely to have been a key influence on the screening and prenatal diagnosis uptake. Further research is needed exploring perceptions of SMA amongst the general population in the UK.
p. 15	The treatment	Given that the research field is very active regarding treatments, what are the anticipated effects, if any, on such research if a screening programme were to be introduced? This issue was not addressed in Cartwright's paper, but will be a key concern of families currently living with SMA.
p. 17	There should be an effective treatment or intervention for patients identified through early detection, with evidence of early treatment leading to better outcomes than late treatment.	It's not clear why an antenatal screening programme appears to being considered rather than a newborn screening programme. Indeed, many of the studies of attitudes towards screening for SMA focus on newborn screening (Rothwell, 2013) and the ethical and social implications of each are vastly different. A justification for the point in time at which the screening occurs needs to be made explicit in the review.
p. 18-19	Population studies on carrier screening for SMA	Ben-Shacher et al.'s (2011) study conflicts with more recent evidence on compliance in this population (Sukenik-Halevy et al., 2012). Whilst Sukenik-Halevy et al. (2012) had a very small sample size compared to Ben-Shacher et al. (2011), the uptake of SMA screening in Sukenik-Halevy et al.'s (2012) study is in stark contrast- 20% uptake compared to 93% in Ben-Shacher et al.'s (2011). Religious beliefs, intention to carry the pregnancy to term irrespective of test results and the perception that the test is not necessary (as it must be paid for rather than being provided through standard antenatal screening) were offered as reasons for this low uptake. There is a general lack of population studies on SMA screening, and none have been undertaken in the UK. This is a serious gap in the literature.

p. 19	There should be evidence that the complete screening programme is clinically, socially and ethically acceptable to health professionals and the public	There exists a wide range of views towards screening for SMA, and much of this diversity can be accounted for by the broadly different presentations of the condition (from very severe and resulting in premature death to relatively mild) and the inability of genetic testing to distinguish between them. Indeed, the possibility of SMA screening raises important questions about how severe conditions need to be in order to justify a screening programme, and who is able to make that judgement. My interview study (Boardman, 2010) discovered that many families, especially those who had experience of Type II or III SMA felt conflicted about using prenatal testing to prevent recurrence in future pregnancies as they felt that SMA could be successfully lived with. Indeed, some parents expressed gratitude that SMA *had not* been detected through antenatal screening, as, before they had experienced SMA first-hand, they would have been more afraid of the consequences of it and three participants stated that they would have terminated the pregnancy had they known antenatally that their child had SMA- a decision that, with their present knowledge, they feel would have been wrong for them, having experienced the reality of SMA through their child. It was not uncommon for such parents to highlight what they would have 'missed out on' had the SMA been diagnosed antenatally and a selective termination decided upon. Furthermore, individuals diagnosed with SMA themselves referred to what has been described in the literature as the 'expressivist objection' (Parens and Asch, 2000); the notion that the prevention of SMA through the use of genetic technologies expresses a negative valuation of the lives of people living with SMA, which was associated with psychological distress and disruption to family relationships (Boardman, 2011). For other participants, particularly those who experienced the premature deaths of their babies due to Type I SMA, screening was perceived as vital and many perceived a burden of responsibility on themselves to prevent the recurrence of SMA, not only within their own families, but within the wider community. There was evidence of strong feelings on both sides of the debate (Boardman, 2014). My current ESRC funded research project, 'Imagining Futures: The Social and Ethical Implications of Genetic Screening', due for completion in 2016, will build on this existing research by exploring the views of families living with SMA

		specifically in relation to population screening for SMA. No previous studies on the views and experiences of families living directly with SMA, and their views around screening, exist. The research study involves 40 in-depth qualitative interviews and a nation-wide survey of families living with SMA who are registered with the Jennifer Trust for Spinal Muscular Atrophy in the UK. Participants will be asked about their experiences of living with SMA, their views around carrier screening and prenatal testing, and questions around what they would want the UK general public to know about SMA. The views and experiences of families and individuals living directly with SMA have a key role to play in any consideration of a screening programme for SMA, as well as the development of any resulting educational materials. The results of this research will be published in peer-reviewed journals, disseminated through academic and patient workshops and conferences, debated in public forums, such as radio talk shows (e.g. Radio 4 moral maze) and websites/presentations for the interested general public (e.g. mumsnet/ café scientifique/ ethnodrama production) and will be key evidence for any future reviews of SMA screening policy. Moreover, it is anticipated that this research will lead on to another study exploring attitudes towards SMA, and carrier screening for SMA, amongst the general public in the UK. A very limited number of studies have explored the attitudes of the general public towards carrier screening for SMA and these have all been conducted in the USA. Inferences are often made about attitudes to SMA and screening based solely upon rates of uptake or refusal of the screening tests, however, detailed analyses that capture the nuances and complexities of public opinion on this topic are lacking. The educational materials that are presented to the general public about SMA in the context of these studies are critical and should not be developed without consultation with families living directly with SMA. As previously stated, Rothwell et al.'s (2013) study of parents' attitudes towards an opt out approach for pilot studies of SMA screening used a video on SMA (available online at: http://learn.genetics.utah.edu/sma/) to show to their participants prior to their focus groups, however the video did not depict adults living with SMA and arguably overstated the ability of screening tests to accurately differentiate between severities of SMA, as well as the benefits of early therapeutic interventions, which may have biased the participating parents' perception of the condition and an opt out approach to screening for it. Similarly,

		the authors stated their own favourable views towards an opt-out approach to pilot studies of screening for SMA at the start of the focus groups, which may also have influenced their results. In the case of Prior's (2010) study of screening (also conducted in the USA), the educational materials provided to members of the general public with no prior knowledge or experience of SMA were developed in conjunction with a pro-screening campaigning group, the Claire Altman Heine Foundation (2009), and copies of their educational materials were not provided in the write up of the study in order for the reader to assess their quality and accuracy. Indeed, it is critical that balanced and accurate information on both SMA and the capacities of screening tests, as well as the limits of therapeutic and curative interventions for SMA, is provided to the general public when attitudes towards screening are assessed so as not to bias results. Moreover, studies need to be conducted with the UK population to allow for social and cultural influences in that particular context. There is a lack of evidence regarding the attitudes of health care professionals towards screening for Spinal Muscular Atrophy more broadly and within the UK specifically. Whilst the American College of Medical Genetics recommends screening, a statement which is at odds with the recommendation *not* to introduce screening at this time by the American College of Obstetrics and Gynaecology, the Association for Molecular Pathology (Muralidharan et al., 2011) takes a more graduated position, arguing that implementation should be in a step-wise fashion, and that critical issues should be carefully and extensively explored prior to full implementation (p.5). Some of the key 'critical' issues that the AMP raises relate to the lack of pilot studies on screening, the lack of correlation between phenol- and genotype for SMA (which is recognised as a large stumbling block in relation to genetic counselling and one which requires further research) as well as the lack of replicative large scale population based studies to estimate carrier frequencies across ethnic groups. The AMP also recommends meetings to engage 'medical experts and other interested parties such as parent groups, researchers, health care providers, ethicists and payers to identify issues, set priorities and develop solutions' (p. 5). It is clear that such community and professional engagement is also required in the UK context. My research project, 'Imaging Futures: The Social and Ethical Implications of Genetic Screening' will provide a springboard for this sort of

		public and professional engagement activities and debate.
p.19	The benefit of the screening programme should outweigh the physical and psychological harm (caused by the test, diagnostic procedures and treatment).	My research will build on my prior research (Boardman, 2010) and explore the perceptions of families living with SMA, many of whom have undergone invasive prenatal testing for SMA and faced extremely difficult reproductive dilemmas. 'Imagining Futures: The Social and Ethical Implications of Genetic Screening' will further explore how families living with SMA conceptualise the potential physical and psychological harms of a screening programme for SMA. It is important that the wider community of adult individuals living with SMA are taken into account when considering the psychological harms of a screening programme. My prior research (Boardman, 2014) highlighted the way in which prenatal testing for SMA could be emotionally challenging for people living with SMA, and these potential and perceived harms will be thoroughly explored and analysed within the research project currently underway.
p. 22	Public pressure for widening eligibility criteria, for reducing the screening interval and for increasing the sensitivity of the testing process, should be anticipated. Decisions about these parameters should be scientifically justifiable to the public.	As Muralidharan et al. (2011) state, a challenge with SMA screening is that genetic testing on additional family members can drastically change risk estimates for family members already tested (p.5). It is therefore possible that screening pregnant women could lead to other family members demanding screening tests e.g. pre-conception screening, particularly if the pregnant woman is found to be carrier. There are serious educational and counselling issues that need to be considered.
p. 22-23	Conclusions	There is a general lack of clarity in Cartwright's report as to whether a pre-natal, pre-conception or newborn screening programme is being assessed. Whilst carrier screening of pregnant women is frequently referred to, the consultation is classified as a 'newborn' screening programme consultation on the UK NSC website, therefore the comments in this policy review document refer to all of these different types of screening. The social and ethical implications of carrier screening for SMA are under-researched and further evidence is needed exploring the way in which families living with SMA, health care professionals and the general public both conceptualise life with SMA and the screening technologies, in the UK context. The general public will be required to make genetic screening and testing decisions in relation to a condition that they are likely never to have heard of, or come across, so it is vital that families and individuals living with SMA are involved in the development of educational materials around SMA. My research, 'Imagining Futures: The Social and Ethical Implications of Genetic Screening' is

		designed to explore the social and ethical dimensions of many of the issues set out in Cartwright's paper and so will be key to any future reviews of this screening policy.

References

Alsulaiman, A., Hewison, J., Abu-Amero, K., Ahmed, S., Green, J. & Hirst, J. (2012). Attitudes towards prenatal diagnosis and termination of pregnancy for 30 conditions among women in Saudi Arabia and the UK, *Prenatal Diagnosis,* 32 (11), 1109-113.

American College of Obstetricians and Gynaecologists. (2009). Committee opinion: Spinal Muscular Atrophy, *Obstetric Gynaecology,* 113, pp. 1194-1196.

Ben-Shachar, S. et al. (2011). Large-scale population screening for Spinal Muscular Atrophy: clinical implications, *Genetics in Medicine*, 13 (2), pp. 110-114.

Boardman, F. (2014). Knowledge is power? The role of experiential knowledge in genetically 'risky' reproductive decisions, *Sociology of Health and Illness,* 36 (3) [in press]

Boardman, F. (2011). Negotiating Discourses of Maternal Responsibility, Disability and Reprogenetics in Lewiecki-Wilson, C. and J. Cellio (ed.s) *Disability and Mothering: Liminal Spaces of Embodied Knowledge,* Syracuse University Press.

Boardman, F. (2010). The role of experiential knowledge in the reproductive decision making of families genetically at risk: the case of Spinal Muscular Atrophy. PhD thesis. Department of Sociology: University of Warwick.

Claire Altman Heine Foundation. (2009). http://www.clairealtmanheinefoundation.org/ Accessed 2/7/13.

Maxwell, S., Kyne, G., Molster, C., Barker, N., Ormsby, J. & O'Leary, P. (2011). Perceptions of population Cystic Fibrosis prenatal and preconception carrier screening among individuals with Cystic Fibrosis and their family members, *Genetic Testing and Molecular Biomarkers,* 15 (3),159-164.

Meldrum, C., Scott, C. & Swoboda, K. (2007). Spinal Muscular Atrophy Genetic Counselling Access and Genetic Knowledge: Parents' Perspectives, *Journal of Child Neurology,* 22 (8), pp. 1019-1026.

Ministry of Health, Israel. (2013). Recommendations for genetic testing http://www.health.gov.il/English/Topics/Genetics/checks/Pages/GeneticTestingRecommendations.aspx Accessed 1/7/13.

Muralidharan, K., Wilson, R., Ogino, S., Nagan, N., Curtis, C. & Schrijver, I. (2011). Population carrier screening for Spinal Muscular Atrophy: a position statement of the Association for Molecular Pathology, *The Journal of Molecular Diagnosis,* 13 (1), pp. 1-6.

Ogino, S., Wilson, R. & Gold, R. (2004). New insights into the evolution of the SMN1 and SMN2 region: simulation and meta-analysis for allele and haplotype frequency calculations, *European Journal of Human Genetics,* 12, pp. 1015-1023.

Opera, G., Kröber, S., McWhorter, M., Rossoll, W., Müller, S., Krawczak, M, Bassell, G., Beattie, C. & Wirth, B. (2008). Plastin 3 is a protective modifier of autosomal recessive Spinal Muscular Atrophy, *Science,* 320, pp.524-527.

Parens, E. & Asch, A. (2000). The disability rights critique of prenatal genetic testing: reflections and recommendations in Parens, E. and Asch, A. (eds.) *Prenatal Testing and Disability Rights* Georgetown University Press: Washington, D.C.

Poppelaars, F., van der Wal, G., Braspenning, J., Cornel, M., Henneman, L., Langendam, M. and ten Kate, L. (2003). Possibilities and barriers in the implementation of a preconceptual screening programme for Cystic Fibrosis carriers: a focus group study, *Public Health,* 117, pp. 396-403.

Prior, T., Snyder, P., Rink,B., Pearl, D., Pyatt, R., Mihal, D., Conlan, T., Schmalz, B., Montgomery, L., Ziegler, K., Noonan, C., Hashimoto, S. and Garner, S. (2010). Newborn and carrier screening for Spinal Muscular Atrophy *American Journal of Medical Genetics* 152 (A7) pp.1608-1616.

Prior, T. (2008). Carrier screening for Spinal Muscular Atrophy, *Genetic Medicine*, 10, pp. 840-842.

Rothwell, E., Andereson. R., Swoboda, K., Stark, L. and Botkin, J. (2013). Public attitudes regarding a pilot study of newborn screening for Spinal Muscular Atrophy *American Journal of Medical Genetics* 161A pp. 679-686.

Russman, B. (2007). Spinal Muscular Atrophy: Clinical classification and disease heterogeneity, *Journal of Child Neurology,* 22 (8), pp. 946-951.

Su Y-N et al. (2011). Carrier screening for Spinal Muscular Atrophy in 107, 611 pregnant women during the period 2005-2009: a prospective based population-based cohort study. *PLoS ONE*, 6 (2) pp. 17067.

Sukenik-Halevy, R., Leil-Zoabi, U. A., Peled-Perez, L., Zlotogora, J. & Allon-Shalev, S. (2012). Compliance for genetic screening in the Arab population in Israel, *The Israeli Medical Association Journal,* 14, pp. 538-542.

Thauvin-Robinet, C., Drunat, S., Veber, P., Chantereau, D., Cossé, M, Cassini, C., Soichot, P., Masurel-Paulet, A., De Monléon, Sagot, P., Huet, F., Antin, M., Calmels, N., Faivre, L., Gérad, B. & Le Réseau Français de Génétique Moléculaire. 2012. Homozygous SMN1 Exons 1-6 Deletion: Pitfalls in genetic counselling and general recommendations for Spinal Muscular Atrophy molecular diagnosis, *American Journal of Medical Genetics Part A,* 158, pp.1735-1741.

Watson, E., Williamson, R. & Chapple, J. (1991). Attitudes to carrier screening for Cystic Fibrosis: a survey of health care professionals, relatives of sufferers and other members of the public, *British Journal of General Practice,* 41, pp. 237-240.