Consultation response on Newborn Screening for Duchenne muscular dystrophy

Muscular Dystrophy UK welcomes the opportunity to respond to the National Screening Committee (NSC) review of Newborn Screening for Duchenne Muscular Dystrophy.

The charity’s response can be summarised as follows:

- Duchenne muscular dystrophy is a severely progressive muscle wasting condition. Progressive weakness is the result of the progressive loss of muscle mass.
- There is now an approved drug for Duchenne muscular dystrophy (Translarna), and a number of others in late stage clinical trial. Consequently, the need to prepare a screening programme that will enable early detection and diagnosis is crucial. As treatments are aimed at protecting muscle from further degeneration, their use in patients is anticipated to be much more beneficial the earlier the age at which they are administered.
- Muscular Dystrophy UK supports screening for Duchenne muscular dystrophy, but recognises that important preparatory work – particularly on the creatine-kinase assay - must be completed to enable NSC approval.
- Muscular Dystrophy UK acknowledges concerns around the reliability of the current screening test. However, it is important to note that a new more sensitive and specific test has been developed by Dr Stuart Moat at the University Hospital of Wales/Cardiff University in collaboration with PerkinElmer and this new test is undergoing an extensive evaluation. Furthermore, a partnership between PerkinElmer and the California Department of Health Newborn Screening Programme is currently underway to develop a more refined screening protocol.
- Given the rapid developments in testing protocol and the fact that there are approved drugs for the treatment of Duchenne, the NSC should be prepared to bring any future reviews for Duchenne screening forward. This would avoid a position where Duchenne screening is ready for approval, but the next NSC evidence review is some years away.
- There is widespread support amongst parents for a newborn screening programme, and most families whose children have been screened report that it was helpful in allowing them to plan ahead and make adjustments to their lives at an earlier stage. This lived experience should be better acknowledged and captured by the NSC.
- Diagnostic delay is still prevalent for Duchenne muscular dystrophy. This means children diagnosed late miss out on best standards of care, leading to worse outcomes than those children who are diagnosed early. Newborn screening would play an important role in addressing the ‘diagnostic odyssey’ and allow timely introduction of standards of care.
- Recent published evidence indicates that in the UK the age at starting steroids (recognised standard of care) is later than optimal, due to frequent delays in the diagnostic process.
- Recent peer reviewed publications suggest that treatment with steroids at an earlier age than the average age of diagnosis is associated with better outcomes. A clinical consensus is emerging around this.
Implementation of best standards of care and treatment

Without any treatment, the natural history of Duchenne muscular dystrophy suggests that patients typically lose the ability to walk before the age of 13 and average life expectancy is in the late teens to early twenties. However, with the right management and best standards of care a child diagnosed with Duchenne in 2016 could live well into their 30s.¹

For newly diagnosed children, treatment will usually include commencement of a corticosteroid regime, which has been shown to prolong ambulation. Given that earlier loss of ambulation is associated with a faster progression of the disease, access to steroids at an early stage is an essential method of treatment and could play a role in prolonging life expectancy.

Professor Francesco Muntoni of the Dubowitz Neuromuscular Centre, says:

“In a child at around the age of five, already one third of the muscle mass has been lost. At the age of 18, normal individuals will have approximately 30 kilograms of muscle; an individual with Duchenne muscular dystrophy will have 1.5 kilograms of muscle. Avoiding progressive muscle loss is of paramount importance for this condition. Anticipatory care is necessary to retain as much function and muscle mass as possible. You don’t wait until there is a big problem and then start finding a way to patch it. When children are diagnosed, they already have been symptomatic. They really have lost a lot of ground…the later you start steroid treatment the less [likely] the steroid will have an effect. So if you start the steroid the day before, for example, or a week before children are going to stop walking, it will have no effect. If you start much earlier, they will prolong the ability to walk for four to five years, which makes a huge difference to subsequent life-expectancy.”

There is a growing amount of evidence in favour of commencing steroids an earlier stage, which Muscular Dystrophy UK does not believe has been properly captured in the NSC’s review.

For example, standardised clinical data analysed through the NorthStar Network found that starting corticosteroids between 3 and 5 years ‘conferred an additional gain in motor function of 3 units/year (in the North Star functional assessment tool) up to age 7’². There is a clear correlation in Duchenne between the level of function and the subsequent loss of motor activities and ultimately respiratory insufficiency and death. Therefore, initiating treatment at an early age – when function is at a higher level – can be expected to confer significant longer term advantage in terms of health outcomes.

Another independent recent study showed that initiation of corticosteroids between 2-4 years showed good long term outcomes after a 14 year observational study.³ There is therefore strong evidence favouring the commencement of steroids at a significantly earlier age than the mean age of diagnosis. Clinical consensus is coalescing around this viewpoint.

It must also be noted that treatments targeting the underlying genetic cause of the disease – such as ataluren – would be expected to be more effective the earlier they are implemented. Licensing restricting use to those aged five and over is an indication of the population who took part in the clinical trials, not because such treatments would be ineffective in younger

¹ Van Ruiten HJA, Straub V, Bushby K et al. Arch Dis Child, September 2014
² Ricotti V, et al. J Neurol Neurosurg Psychiatry 2016 87:149-155
children, and indeed this point was discussed at a recent EMA workshop on standards of care and experimental therapies for DMD (Lancet Neurology). PTC Therapeutics is planning limited safety studies in infants, to confirm the safety and pharmacokinetics of the drug.

Given the probability that more drugs will come ‘on stream’ in the future, ensuring preparedness for newborn screening is essential (see also P.4 ‘revising the testing protocol’). The NSC must therefore be prepared to bring any future review for Duchenne forward should further treatments become available and a revised and commercially available test be in place.

**Diagnostic delay**

Diagnostic delay is a crucial issue affecting the diagnosis and management of Duchenne muscular dystrophy.

Parents and early years professionals are usually the first to spot developmental delay, such as difficulties in getting up off the floor or an inability to keep up with friends or siblings. This is typically between the ages of 2-3 years old although in some instances symptoms may become apparent earlier.

Average age of diagnosis is 4.5 years old, and diagnosis later than this age is prevalent, indicating a significant delay from first reported parental concerns to diagnosis. This is primarily due to a lack of awareness of the disease amongst professionals involved in primary care, who may make an incorrect referral or initially misdiagnose the condition.

The diagnosis of Duchenne muscular dystrophy is devastating for families, and can be made all the worse if it follows months and years of such uncertainty.

Diagnostic delay affects subsequent access to the care pathway and implementation of best standards of care. This means there is delayed access to specialist physiotherapy, regular monitoring by specialists and often boys start steroids later than recommended, or in some instances are unable to begin steroid treatment if they have been diagnosed too late.

Lack of diagnosis can also lead to a lack of appropriate support at school, and in other aspects of day to day life. This can have an impact on cognitive and behavioural development.

Jane Field, whose son, Murray, was diagnosed with Duchenne muscular dystrophy aged 7 and a half, said:

“My son, when he was diagnosed, was seven and a half years old. Therefore he missed out on essential steroid treatment— not really bringing into it the enormous distress that was caused by the lack of diagnosis within his schooling and everything else… I can only speak from my own point of view, and having a son diagnosed at seven and a half is horrific. We didn’t know why he couldn’t walk down the stairs fast enough; the dyslexic problems; the behavioural problems…it was unutterably awful.”
Muscular Dystrophy UK believes that neo-natal screening would play a central role in addressing the ‘diagnostic odyssey’ in Duchenne muscular dystrophy, and allow children to access best standards of care at an earlier stage of the process.

**Revising the testing protocol**

Muscular Dystrophy UK fully recognises the concerns around the reliability of the current assay for Duchenne newborn screening. The creatine-kinase test is prone to a relatively high rate of ‘false positives’, and in Wales the number of ‘false negatives’ the test produced was close to 20%.

This represents a significant barrier to NSC approval for newborn screening for Duchenne, and it is essential that the assay is revised in order to enable screening to move forward.

Following the experience of the Wales programme Dr Stuart Moat has developed a more sensitive and specific screening test in collaboration with PerkinElmer.

We strongly support the work being led by PerkinElmer\[1\] in partnership with the California Department of Health Newborn Screening program to refine the screening protocol for Duchenne muscular dystrophy.

We also recognise the work that Parent Project Muscular Dystrophy \[2\] are undertaking in this area. Muscular Dystrophy UK is committed to supporting this work and to ensuring that steps can be taken to ensure screening can be implemented in the UK.

Further information on the new skeletal muscle specific creatine kinase screening test is available [here](#).

**The family experience**

Whilst there has never been a UK-wide programme of newborn screening for Duchenne muscular dystrophy, a screening programme was in place in Wales between 1990 and 2011 before it was withdrawn.

This means there are a number of children and young adults in Wales who were diagnosed through newborn screening, and whose parents are able to comment on the effects this very early diagnosis had on the family. For many of these families, the choice to screen and the early diagnosis was helpful in enabling them to plan ahead and make important adjustments to their lives, even in the absence of now approved drugs, such as ataluren.

Jeanette and Chris George’s son, Alex, was diagnosed via newborn screening in Cardiff and the family are supportive of neo-natal testing for the condition.

**Jeanette says:**
Having a very early diagnosis was a positive because it has allowed us to plan. We can take holidays that we wouldn’t be able to take with an older boy. We can move into accommodation. We have a nice family home with plenty of space, but if we want to have a purpose-built area for Alex, we can do that before Alex begins to think that we are moving out because of him. We can plan and put things in place; I changed my career. I think with an early diagnosis, we can try and spend more time at home, taking the positive out of it. Alex gets assessed every six months, so any change in his wellness will be picked up immediately. He has taken steroids from the age of four."

Chris says:

"The positive result and the immediacy of having to face up to the diagnosis of a little boy who appeared to be physically fine was initially traumatic, but we cannot emphasise enough how the early diagnosis has helped us cope, plan and nurture Alex in the knowledge of his condition."

Other families working with Muscular Dystrophy UK – whose children were not screened – also feel that they would have preferred to have received a diagnosis through newborn screening.

Penny Southall, whose son, Dan, was diagnosed aged 3, says:

"Speaking as a mum who has a boy with Duchenne muscular dystrophy, there’s never going to be a ‘good’ time to find out. But I strongly believe that once you have a diagnosis, you can take positive steps to help your child. I feel that it is in the boys’ best interests to be diagnosed as soon as possible, so that they can receive the support they need - as soon as they need it.

Giving parents the opportunity to screen their child can give them precious extra time to think about the implications of trying for another child, where to live, and where their son should go to school. It is devastating to find out that your longed-for and loved child has a condition like Duchenne, but I think we need to accept that the benefits of an early diagnosis are well worth having."

Monica Morwood, whose son, Michael, was diagnosed with Duchenne aged seven-and-a-half, says:

"The diagnosis was devastating, the loss of the healthy child we thought we had. If we had known earlier we would have had more time to plan housing and think about Michael’s education. We would have moved earlier. We still would have been devastated and grieved, but would have found out how to manage the condition and would have made
the best of those early years. Given there have been so many advances in research and management of the condition, the outlook for boys with Duchenne muscular dystrophy has improved tremendously. Even without a treatment available right now, having the choice to screen your child could make a profound difference to their quality of life, as early management is so important.”

However, it must be acknowledged that not all families have the same point of view, including those who experienced newborn screening in Wales.

John Burke’s son, Seth, was diagnosed via newborn screening. He strongly feels that in the absence of effective treatments administered in early life, a neonatal diagnosis was the wrong time at which to be told his child has Duchenne.

“... My son was picked up as part of the newborn screening testing in Wales. We had no information about the screening process before the test being done. We were in hospital for one day; it was our first child and we were offered it under the premise that it always comes back negative ... It is the worst thing that we have done to sign the consent form for the test. It is a cruel and unusual torture. The test has no backbone to it; it is performed by one professional, early diagnosis is given by a different set of professionals; there is no overriding person who sees you through the process ... You get an early diagnosis at six weeks but we can only get an appointment with a neuromuscular consultant once Seth starts to become symptomatic. We have a diagnosis but we can’t do anything with it.”

The Burke family’s experience also highlights the need to ensure that sufficient numbers of neuromuscular care advisors are in place to support parents whose infant son has just been diagnosed. Families face huge challenges coming to terms with a diagnosis and will need to know what support is available and where to find it. Appropriate and robust support for families will be a crucial component of any newborn screening programme in the UK.

Surveying family views on newborn screening

During the previous NSC consultation period on newborn screening, Muscular Dystrophy UK, in partnership with the Duchenne Family Support Group and Action Duchenne, conducted a survey to ask the opinion of families affected by Duchenne muscular dystrophy.

In total, 255 people from the UK participated in the survey, 17 of whom were from Wales and had participated in the newborn screening programme for Duchenne muscular dystrophy.

We sought to find out if people supported the introduction of a newborn screening programme now, in the absence of effective or curative treatments. We also wished to see what effect the introduction of such treatments for Duchenne muscular dystrophy might have on support for a newborn screening programme.

The survey results showed that:

- 82 percent were in favour of a newborn screening programme even without an effective treatment to prevent the development of symptoms
- 97 percent of people were in favour of newborn screening if effective treatments were available.

Comments from respondents included:

“[I would support it] wholeheartedly. Currently knowing there is no treatment for Duchenne muscular dystrophy is similar to telling parents their child has an incurable cancer. Whereas
if there is a known treatment then the sooner diagnosis is made the quicker treatment can start.”

“I would support it regardless of current available treatments. Newborn screening would prevent boys from falling through the net and [would] ensure that they could get the help they need as soon as possible.”

When to screen?

Current steroid treatment for Duchenne muscular dystrophy is not administered before the age of two and new treatments may not be given to babies. Therefore, the survey looked to find out parents’ views on the time at which they would have preferred to learn of their child’s diagnosis:

- 53 percent of parents said they would prefer to know soon after birth
- 28 percent of parents said they would prefer to know once their child started showing symptoms
- 19 percent of respondents didn’t know when a preferred time would be.

Those in favour of knowing soon after birth felt it would have helped them to plan for the future, plan future pregnancies and access the full range of therapies. Comments included:

“As soon as possible would be best because you can be prepared for what changes you will have to make for your family life.”

Some felt they could have been better parents had they known earlier:

“Speaking to other mums who did not have the diagnosis early, they felt guilty, thinking their child was lazy when they were tired due to their condition and sorry that they reprimanded him at times when he was not at fault.”

Others would have liked to have known at birth because they found getting a diagnosis later on very stressful:

“I personally would have liked to have known soon after birth because for me, feeling something was wrong and always pressuring my GP and health visitor for a referral was a very difficult time.”

“If screening had been available when my son was born, an early diagnosis could have been made. I could have made better choices about health and education. I could also have found a more suitable home location and secured better support from social services.”

For those who would have preferred a diagnosis when symptoms arose, their view was largely informed by the stress-free time they would have had prior to diagnosis:

“We had six wonderful years of blissful ignorance in which to enjoy our two young boys.”

Several people commented that they felt the timing of newborn screening was wrong:

“I feel newborn is too early and at signs of symptoms is too late, if steroid treatment can be given as early as two to three years old, then testing may be better around then,” and “knowing soon after birth could rob a child of some ‘normal’ interaction and bonding with family.”

Informed consent and post-diagnosis support
Parents reiterated their concerns about the necessary support being available at diagnosis. This was mirrored in the responses from families in Wales who participated in newborn screening for Duchenne muscular dystrophy, many of whom said there was a lack of support and information throughout the diagnostic process:

- only two in five respondents felt they received enough information about the heel prick test when making a decision to participate in the screening
- nearly a third of respondents were unaware their baby had been screened for Duchenne muscular dystrophy
- half of respondents said the consent process could be improved
- only one in three parents felt they received enough professional support during the diagnosis process, with many being left to seek out information themselves on the Internet and from charities.

Several respondents, however, praised the help they received:

“*I cannot fault the support that we had at the time, or the support since.*”

To follow up on this, we asked families from all over the UK what information they thought should be provided to parents to help them make the decision to take part in Duchenne muscular dystrophy newborn screening programme if it were offered, and by whom, when and how. Almost all respondents wanted a full and comprehensive description of the effects of Duchenne muscular dystrophy and of which treatments could be administered if their child were diagnosed shortly after birth. Respondents differed in their view of who should deliver this information, but common responses included specialists on Duchenne muscular dystrophy, as well as neuromuscular care advisors.

*For more information on Muscular Dystrophy UK’s work on newborn screening for Duchenne muscular dystrophy, please contact Peter Sutton on p.sutton@musculardystrophyuk.org or call 020 7803 4838.*