Newborn screening for spinal muscular atrophy (SMA) should be an urgent priority to radically improve outcomes for affected children and their families, as well ensuring a cost-effective approach to the use of transformational but expensive treatments – April 2023

Key messages

- Every five days in the UK, a baby is born with spinal muscular atrophy (SMA).
- Spinal Muscular Atrophy (SMA) is a rare, genetic neuromuscular condition causing progressive muscle wasting and weakness leading to loss of movement. This may affect crawling and walking ability, arm, hand, head and neck movement, breathing and swallowing. There is a wide spectrum of how severely children and adults are affected.
- In the last three years, the NHS has revolutionised care for those who have SMA by funding access to three ground-breaking treatments - Nusinersen (Spinraza™), Onasemnogene abeparvovec (Zolgensma™) and Risdiplam (Evrysdi™). This has been life-saving for babies with the most severe SMA Type 1, who previously would have died before the age of 2 years. 60% of those diagnosed each year have SMA Type 1.
- If these treatments are delivered prior to symptom onset, better health outcomes can be achieved and most would benefit from typical neuromuscular development.
- There is no newborn screening for SMA in the UK, and many are missing the opportunity to be treated pre-symptomatically.
- Once an infant shows overt symptoms of SMA, there is already irreversible damage to the nervous system which affects muscles and movement. This causes complex and lifelong health challenges, increasing the overall costs of managing the condition significantly.
- This is why many European countries have moved quickly to approve SMA newborn screening. It is unethical that UK families are unknowingly denied access to this critical treatment window when we have a safe, cost effective and efficient test for SMA.
- Newborn screening is the fastest route to a diagnosis of SMA and should be introduced today. It is unethical to delay.
- The UK NSC review of newborn screening for SMA has now begun but progress is slow and there is scope to expedite a robust decision by:
    - Using existing economic modelling to understand whether screening for SMA is clinically and cost effective;
    - Rapidly quality assuring the existing model by drawing on the expertise of the model authors to understand assumptions and sources; and
    - Taking findings of the modelling work to the UK NSC committee meeting in June 2023 to allow for an “in service evaluation” to be agreed and commenced in the Autumn.

What is SMA?

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Why is newborn screening so important for SMA?

- Once an infant starts showing symptoms of SMA, there is already irreversible damage to the nervous system, which affects muscles and movement.
- Even when treatment is initiated once symptoms have appeared, most of these infants will never walk independently and many will need mechanical ventilation, nutritional support and 24/7 care.
- This represents a high cost to children and their families, the NHS and society.
- Conversely, when treatment is given before a baby shows any symptoms – something made possible through newborn screening – those children can experience a life without severe and progressive weakness. For babies already showing symptoms at birth, newborn screening offers the earliest possible intervention and therefore the best possible outcomes from treatment.

What treatments are available?

- Three life-changing treatments – Nusinersen (Spinraza™), Onasemnogene abeparvovec (Zolgensma™) and Risdiplam (Evrysdi™) – are now funded by the NHS.
- In March 2023, NICE also approved the use of Zolgensma for treating presymptomatic SMA in babies.
- These groundbreaking treatments have been life-saving for babies with the most severe SMA, who previously would have died before the age of 2.

What is the current status of newborn screening for SMA in the UK?

- SMA is not currently one of the conditions screened for through the NHS newborn blood spot screening programme – better known to parents as the “heel-prick test”.
- Newborn screening for SMA is currently only available to siblings of children with SMA, which represents a very small number of those babies diagnosed each year.
- In 2018, newborn screening for SMA was rejected in the UK, partly due to treatments not then being routinely available on the NHS.
- In November 2022, the UK National Screening Committee (UK NSC) announced that it would undertake a fresh review of newborn screening of SMA.
- This process includes a review of existing evidence and research regarding the efficacy and cost-effectiveness of newborn screening for SMA.
- As part of its decision-making process, the UK National Screening Committee (UK NSC) considers economic modelling to be important for rare diseases, given the limitations on available evidence.

What has changed since the last UK NSC of SMA?

- As well as the advent of revolutionary new treatments, an increasing number of European countries and almost all US States (48/50) have introduced newborn screening for SMA. This means that there is a wealth of evidence supporting the need and demonstrating the clinical and cost effectiveness of newborn screening. Some UK-specific evidence is set out below.
- UK SMA Newborn Screening Alliance Chair, Laurent Servais, has worked with others on an economic model that evaluates the cost effectiveness of newborn screening for SMA in England and Wales, versus not introducing newborn screening for SMA. This model has shown that:
    - The introduction of newborn screening for SMA in England and Wales is estimated to identify approximately 96% of cases of SMA in infants per year;
    - Introducing newborn screening would be less costly and more effective than not introducing it;
    - Introducing newborn screening for SMA would result in savings of over £62million over the course of the lifetime of the cohort of newborns diagnosed with SMA each year; and
    - There would be an estimated gain in quality-adjusted life years (QALYs) of 529 years over the lifetime of this cohort.
- There is also research underway to increase understanding about the implementation of newborn screening for SMA and to assess its acceptability to families and the wider UK population.
    - The Thames Valley Pilot for Newborn Screening for SMA offers the opportunity for newborns to be screened for SMA across four Trust sites. Initial findings from this ongoing study have shown that out of 4,000 babies screened for SMA between June-December 2002, there has not been a single false positive returned from SMA screening, reflecting the maturity of the screening methodology.
    - University of Warwick is conducting a study on acceptability of newborn screening for SMA: the initial pilot survey from this study showed 88% of respondents being in favour of the introduction of newborn screening for SMA.
- All available research provides strong support for the UK NSC to deliver a positive decision for newborn screening for SMA
- Separately, Genomics England is running a Newborn Genomes Programme, which aims to deliver a study to sequence the genomes of over 100,000 newborns. Whilst whole genome sequencing for newborn screening holds great potential, this will have a longer timeline for implementation as its implications and ethical considerations are worked through. The current approach plans to deliver an academic study rather than an ongoing solution, so the need for adding SMA to the existing “heel-prick test” remains urgent.

What is the UK SMA Newborn Screening Alliance asking for?

- For every five days that a decision on newborn screening for SMA is delayed, a new baby is born with SMA and will be denied the chance of a healthier future.

- The UK NSC process is underway but there is a lack of clarity on the process and timelines associated with a decision being made.
- There were delays to the initiation of the review and, whilst we do not want to undermine the robust nature of the UK NSC approach, there is huge scope for the assessment to be more ambitious in terms of timelines.
- UK NSC should use the current review of SMA to demonstrate the flexible and innovative approach to decision-making on newborn screening that was promised via the Rare Disease Action Plan.
- We believe that the UK NSC can expedite its process and timelines without compromising on rigour through:
    - Agreeing to use the existing newborn screening cost effectiveness model for England and Wales to understand the clinical and cost effectiveness of newborn screening in the UK.
    - Rapidly quality assuring the assumptions made in the model, drawing on the model authors' expertise to increase understanding at an early stage.
    - Taking the model and a recommendation for a national "in service evaluation" (pilot) of SMA to the UK NSC as soon as possible (i.e. June 2023 meeting)
    - Swiftly commencing a national in-service assessment (i.e. a pilot) to ensure that newborn babies are offered the chance of life-changing screening at the earliest opportunity in a fair and equitable way.

Case study: Maisie and Amelia's story

Following symptoms at 4 weeks old, Maisie was diagnosed with SMA at 6 weeks of age. Her family was informed that her SMA was likely to be very severe. Without treatment, Maisie probably wouldn't have seen her first birthday. However, through access to Spinraza, Maisie is now 4 years old and lives a full and exciting life. She is now also eligible to receive Zo lgensma.

It's not a life without challenges, however. Maisie's weak respiratory muscles mean that her daily routine involves twice-daily respiratory physiotherapy. She also has to use a ventilator when sleeping and even a common cold can result in a hospital stay.

Due to Maisie's diagnosis, her parents had access to prenatal testing when pregnant with Maisie's younger sister Amelia, which confirmed she had SMA. Amelia received pre-symptomatic treatment for SMA at 10 days old and is continuing to develop normally as a result of this early intervention.