



All Party Parliamentary Group for Muscular Dystrophy

Newborn Screening for Rare Conditions

May 2023

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Foreword

Newborn screening is a vital tool for achieving timely diagnosis of rare conditions. With access to treatments and other health and care support advancing for some rare diseases over recent years, the importance of this timely diagnosis has become ever-more critical for people living with neuromuscular conditions and other rare conditions.

We have heard powerful testimonies about the need for changes to the current approach to the assessment of rare conditions for inclusion in the UK newborn screening programme. As this report shows, the processes and criteria used by the UK National Screening Committee (UK NSC) to make decisions on the conditions that are screened for are not currently meeting the needs of the rare disease community. Under the current system, it is difficult to demonstrate and advocate for the need to screen newborn babies for a rare condition – resulting in babies with rare conditions missing out on the potential for faster diagnosis and quicker access to healthcare and treatment.

We have seen how this can have a negative impact on health outcomes – severely affecting not only individuals living with a condition and their families, but also an already strained health and care system.

This inquiry report seeks to set out what best practice approaches to assessing rare conditions for newborn screening could look like and makes recommendations as to how these could be addressed and implemented. The experts who contributed to this report are well placed to support the UK NSC as it seeks to deliver the ambition set out in the Rare Diseases Action Plan for England 2023 of “improving how decisions are made on newborn screening for rare conditions”¹ for the benefit of those affected, the NHS and the UK's performance in newborn screening relative to other countries.

We hope that by highlighting these recommendations to the UK NSC and other key decision makers, we can find a way to move past the situation whereby we have a newborn screening assessment process that is not meeting the needs of people with rare conditions, and the UK can come more into line with other comparable countries when it comes to newborn screening. The inquiry has resulted in recommendations that would help to ensure an appropriate level of pragmatism for considering rare diseases for newborn screening whilst retaining a robust assessment process. We hope that this report is able to inform the work of the Blood Spot Task Group (a group set up to identify practical and innovative approaches to developing evidence for consideration by the UK National Screening Committee).

We would like to thank everyone who has contributed to this inquiry, both at the evidence sessions and in submitting written evidence. We know that there are parliamentary colleagues who are extremely interested in this topic and how it progresses, and so we look forward to seeing how these recommendations may be taken onboard to deliver effective change.



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¹ www.gov.uk/government/publications/england-rare-diseases-action-plan-2023/england-rare-diseases-action-plan-2023-main-report

Muscular Dystrophy UK

Muscular Dystrophy UK is the charity bringing individuals, families and professionals together to beat muscle-wasting conditions.

Founded in 1959, we have been leading the fight against muscle-wasting conditions since then.

We bring together more than 60 rare and very rare progressive muscle-weakening and wasting conditions, affecting around 110,000 children and adults in the UK.

- We support high-quality research to find effective treatments and cures and won't stop until we have found them for all muscle-wasting conditions.
- We are leading the drive to get faster access to emerging treatment for families in the UK.
- We ensure everyone has the specialist NHS care and support they need – the right help at the right time, wherever they live.
- We provide a range of services and resources to help people live as independently as possible.

**Muscular
Dystrophy UK**

Fighting muscle-wasting conditions



www.muscular dystrophyuk.org

Registered Charity No.205395 and Registered Scottish Charity No. SC039445

The All-Party Parliamentary Group for Muscular Dystrophy

The All-Party Parliamentary Group (APPG) for Muscular Dystrophy, chaired by Mary Glendon MP, is a cross-party group of MPs and Peers in the Houses of Parliament. Its role is to raise awareness of all types of muscle-wasting conditions and promote links between parliament, individuals and families affected by these conditions, charities and scientists, health professionals and decision-makers.

Acknowledgements

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The APPG for Muscular Dystrophy also wishes to thank the All-Party Parliamentary Group for Rare, Genetic and Undiagnosed Conditions for supporting the inquiry.

Muscular Dystrophy UK and the APPG want to thank all contributors to the evidence collection.

The Officers of the APPG for Muscular Dystrophy are:

- Mary Glendon MP (Labour, North Tyneside) (Chair)
- Jim Shannon MP (Democratic Unionist Party, Strangford)
- Baroness Thomas of Winchester (Liberal Democrat)
- Liz Twist MP (Labour, Blaydon)
- Steve Brine MP (Conservative, Winchester and Chandlers Ford)

Executive summary

In England, the newborn blood spot test is carried out to screen for nine conditions, with a tenth condition, tyrosinaemia, recommended in February 2023. Other countries in Europe with similar health systems screen for many more than this (~20) whilst the US screens for up to 50. The UK NSC published a blog in February 2023 which rejected ‘simple comparisons’ between countries on approaches to newborn screening². The blog cites the UK NSC’s rigorous approach to avoid potential harm – but as this report will outline, the potential benefits of newborn screening risk not being fully realised without a more pragmatic approach being adopted.

Many in the rare disease community see newborn screening for rare conditions as a vital tool for ending what is known as the ‘diagnosis odyssey’ (delay in diagnosis leading to delay in appropriate management and treatment of a condition, which may cause further deterioration of health).

In October 2022, the All-Party Parliamentary Group (APPG) on Muscular Dystrophy launched an inquiry into newborn screening for rare conditions and the evidence requirements for the acceptance of a condition onto the national newborn screening programme. The inquiry was supported by the APPG on Rare, Genetic and Undiagnosed Conditions.

In parallel to the establishment of this inquiry, the Blood Spot Task Group (BSTG) was established to encourage a more practical and innovative approach to evidence requirements for newborn screening assessments to ensure that they are appropriate for rare conditions. The inquiry was designed to help to inform the BSTG’s thinking on this important topic.

Inquiry terms of reference

The APPG inquiry aimed to understand:

- The views of people living with rare conditions on the potential impact of newborn screening on families, society and the NHS.
- The types of evidence that should be considered to allow robust but timely decision-making about adding rare conditions to the UK national screening programme, and how uncertainty arising from evidence relating to rare conditions should be handled by the UK NSC.

The Inquiry focused on:

- The current approach taken by the UK NSC to reviewing rare conditions for newborn screening, such as the length of the review process.
- The criteria that a condition must currently meet to be considered for newborn screening and the evidence requirements to support an appropriate expansion of the list of conditions screened for. A particular focus was the extent to which these requirements are fit for purpose for rare conditions.

² <https://nationalscreening.blog.gov.uk/2023/02/15/simple-screening-comparisons-between-countries-mask-complex-differences/>

- The value of involving condition specific stakeholders in the UK NSC assessment process and how this can best be achieved.

Whilst the inquiry looked at newborn screening for rare conditions overall, there was a specific focus on spinal muscular atrophy (SMA), given the announcement in November 2022 by the UK NSC that work had started on reviewing newborn screening for SMA.

This report discusses inquiry findings and makes recommendations based on these findings. We hope that the recommendations are considered by the UK NSC Bloodspot Task Group when thinking about evidence for decision making on blood spot screening for newborns.

Methodology

The inquiry launched in October 2022 and continued until February 2023. It gathered feedback and recommendations from a range of rare condition stakeholders, in the following ways:

- An online survey, mainly comprised of open text box responses. Twenty-eight responses were received.
- Eight in-depth interviews with stakeholders from the rare disease community including clinicians, academics, health policy specialists, health economist and advocacy group representatives.
- A roundtable discussion with a range of patient organisations and clinicians (10 in total) with experience of rare conditions.

Overall, we heard 46 different evidence contributions.

Background

In January 2021, the UK Rare Diseases Framework was published which laid out four priorities aimed at improving the experiences of people living with rare conditions. The first of these priorities is helping patients to get a final diagnosis faster. This is mirrored in the England Rare Diseases Action Plan, published in February 2022.

Both the Framework and the Action Plan acknowledge that timely and effective diagnosis can provide important options in terms of treatments for, and management of, rare conditions. They also highlight how receiving a final diagnosis ends what is known as the ‘diagnostic odyssey’ – recognition of the fact that the process of receiving a confirmed diagnosis is particularly challenging for the rare disease community, who experience long waits, uncertainty, multiple referrals, and sometimes incorrect diagnoses. For some people living with a rare disease, especially those with progressive conditions, this is a time in which their condition may deteriorate, or, vitally, key windows for the most effective intervention are missed.

The England Rare Diseases Action Plan in particular also states that alongside great personal cost, research from 2018 estimated that, over a 10-year period, the ‘diagnostic odyssey’ for rare diseases has cost NHS England in excess of £3.4 billion³.

The UK National Screening Committee (UK NSC) is responsible for assessing the evidence for national screening programmes and recommending which conditions should be screened for.

³ https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1057534/England-Rare-Diseases-Action-Plan-2022.pdf

In the case of certain conditions, diagnosis and treatment with disease modifying treatments at the earliest possible opportunity can limit or prevent the development of symptoms. However, in the absence of newborn screening for a condition not currently included in the Newborn Screening Programme there is currently no mechanism in place in the UK to detect these conditions prior to symptoms emerging, except in the small number of cases of known family history.

The Rare Disease Framework describes the aim of newborn screening as being:

“To detect and provide further tests or treatment at an earlier stage with the objective of improving outcomes”.

In recognition of ongoing challenges surrounding the assessment of the appropriateness of adding individual rare conditions to the newborn screening programme, the England Rare Diseases Action Plan (2022) made a commitment to improve the way decisions are made on newborn screening for rare diseases. This would be achieved through the establishment of a UK NSC Bloodspot Task Group, which was set up to identify approaches to facilitating evidence to inform evaluations of blood spot screening; and more engagement and learning from international best practice for newborn screening.

Summary of recommendations:

The inquiry showed support for the UK NSC to continue to take a robust approach to assessing the appropriateness of conditions for newborn screening. However, there was consensus that there was scope for a significantly faster, more transparent approach that takes factors such as the progressive nature of many rare conditions, and the significant associated health implications for babies born with them, into greater account. Receiving a prompt and accurate diagnosis is crucial to ensuring appropriate and informed treatment decisions and/or management and care decisions can be made. Yet it is well documented that babies born with rare conditions often face significant delays in diagnosis. There are some rare conditions where newborn screening is an appropriate method of providing a faster diagnosis.

The emergence of disease modifying treatments for some rare conditions, which can have optimal impact if administered at the earliest opportunity, has added even more importance to the UK NSC taking an approach which facilitates timely assessment of conditions for newborn screening, which is in sync with the development of these new treatments.

After highlighting issues around the current approach for assessing rare conditions for newborn screening, inquiry participants made a range of suggestions as to how this could be improved so that it was fit for purpose for the conditions being assessed.

The recommendations fall into three overarching themes, with specific recommendations within each category. The main body of this report covers these recommendations in detail; however, they are also summarised below.

The approach taken by the UK NSC to assessing conditions for newborn screening needs to be expedited. Whilst it should be robust, there are ways in which it could be more pragmatic.

Evidence gathered in the inquiry highlighted several ways in which a more pragmatic approach to assessing conditions for newborn screening could be implemented. These included:

- When conditions previously rejected for newborn screening are reassessed, there should be a clear, expedited process in place that demonstrates how gaps will be filled, rather than starting the review process from scratch each time. These reviews should be quicker given the existing work already done.
- Effective horizon scanning should inform UK NSC scheduling to facilitate newborn screening decisions being more closely aligned with NICE recommendations. The UK NSC should review how independent or academic pilots are being proposed and run so that they can engage with stakeholders to ensure that the initiation, purpose, and implementation of pilots are based on a shared and jointly understood goal: to assist meeting evidence criteria.
- The UK NSC should benchmark its approach to economic modelling to ensure that processes and timelines are more ambitious and aligned with agreed best practice.
- The UK NSC should consider international evidence from countries with similar health systems that offer robust national newborn screening programmes for certain conditions.

The criteria and evidence requirements for a condition to be accepted for newborn screening need to be reviewed so that they are fit for purpose for rare diseases.

- The current criteria should be reviewed to ensure that evidence requirements are appropriate for rare conditions, as is seen in other health technology assessor approaches.
- The UK NSC should align its approach to evidence requirements with regulators and health technology assessment bodies so that it avoids duplication in evidence assessment and the associated burden placed on rare condition stakeholders to produce evidence for multiple different assessments of the same condition.
- The UK NSC should take into account real world evidence, such as data about treatments collected via Managed Access Programs which demonstrate the clinical effectiveness and impact of intervention.

A clear and transparent approach focused on stakeholder engagement is key.

- The UK NSC should involve stakeholders at all stages of the assessment process.
- The UK NSC should take a more proactive approach to identifying conditions for newborn screening.
- The UK NSC should publish timelines for the review of a condition for newborn screening, clearly setting out formal opportunities for stakeholder engagement.
- The UK NSC's performance against timelines should be monitored and made publicly available.
- The UK NSC should adopt examples of best practice in transparency and stakeholder involvement from other organisations.
- The UK NSC's resources and remit should be reviewed by the Chief Medical Officer so it is equipped to fully connect with the rare disease regulatory landscape and rare disease stakeholder communities.

Evidence and recommendations in detail

Chapter 1: An expedited approach to assessing conditions for newborn screening that is robust yet pragmatic.

1.1 Perceptions of the current approach taken by the UK NSC:

A key theme to emerge from the inquiry was widespread concern that the current approach taken by the UK NSC to assessing a condition for newborn screening is too slow. Inquiry participants felt that the approach does not take into account factors such as the progressive nature of many rare conditions and the significant associated health implications for babies born with them. This is crucial, as without a diagnosis there cannot be fully appropriate management of a condition or access to emerging disease modifying treatments, where these are available.

“The current approach makes the process for rare disorders an extremely long process which is really not fit for purpose”

– A clinician who specialises in rare diseases.

For example, it was highlighted that the UK NSC received a submission to screen for Metachromatic leukodystrophy (MLD), in December 2021. In Autumn 2022, the UK NSC said it would consider MLD in its work program for 2022-23. It seems that it has taken approximately a year for the Committee to begin reviewing MLD.

1.1.2 The resource and remit of the UK NSC

Many participants noted resource within the UK NSC as a potential barrier to desired methods and processes.

We needed to see the NSC and their team (programme management team) were fully and properly resourced and I don't think that has happened for many years in terms of doing the job that we are asking – to proactively work with different patient groups and other regulators to become quicker and more agile in terms of considering conditions for screening.

– An advocacy group/patient organisation roundtable participant

Equally, representatives of some conditions mentioned that it is unclear why newborn screening is considered by the same body that considers more general population screening for conditions like breast screening and prostate screening. The introduction of the Blood Spot Task Group is seen as welcome in the sense that this will be a group which specifically oversees, and can focus on, newborn screening.

It was felt that if there is a limited budget available to the UK NSC, then a prudent investment would be to take into account the methods and processes recommended in this report.

1.2 The importance of the UK NSC assessing conditions for newborn screening in a timely manner:

Many people living with a rare condition face significant challenges getting a diagnosis.⁵ Genetic Alliance UK has reported that over a third of people with a rare condition have to wait more than five years for a confirmed diagnosis. Within the rare disease community this is commonly referred to as the ‘diagnostic odyssey’, which is the delay from suspecting someone has a condition through to being able to confirm this via a diagnosis.

This issue has been further exacerbated by the COVID-19 pandemic. Muscular Dystrophy UK’s 2021 report on the impact of COVID-19, ‘Shining a light⁶’, highlighted the disruption to diagnosing neuromuscular conditions in the UK, with 38 percent of people having to cancel new face-to-face diagnosis appointments; and 72 percent experiencing delays in DNA analysis required for diagnosis.

Receiving a prompt and accurate diagnosis is crucial to ensuring that appropriate and informed treatment decisions can be made, and that management and care approaches can be properly tailored to a specific condition. Delays in this process can have severe adverse effects on the physical and mental well-being of people living with rare conditions and their families.

Many rare conditions are complex, multi-system conditions that require ongoing management by a team of specialist multi-disciplinary professionals. Yet, if a baby is not promptly diagnosed with a specific condition, they are unable to benefit from this level of care, which has significant implications for their health, and the well-being of their wider family. This in turn has significant implications for the health and care system. A report published in 2017⁷ found that unplanned hospital admissions amongst people living with neuromuscular conditions were disproportionately high amongst those who did not have a confirmed diagnosis, compared to those who had a diagnosis and were known to specialist neuromuscular teams. Amongst the paediatric sample, most unplanned admissions and many admissions that resulted in an ICU stay were those who had not yet had a diagnosis.

Crucially, the increasing availability of disease modifying treatments for some rare conditions adds greater need to expedite assessments of conditions for newborn screening. Frequently, it is accepted that the optimum window for efficacy of such treatments is prior to a baby developing symptoms of the associated condition. However, in the absence of newborn screening, most babies are only diagnosed once they show symptoms and even then, families can face a lengthy wait for a confirmed diagnosis. This can have a significant adverse impact on long-term outcomes for babies who are eligible for treatment but not able to access it during the most crucial time period – as early as possible, potentially prior to displaying symptoms.

5 <https://geneticalliance.org.uk/wp-content/uploads/2022/02/Rare-Disease-UK-Good-Diagnosis-Report-2022-Final.pdf>

6 https://www.muscular dystrophyuk.org/static/s3fs-public/2021-07/POL14%20-%20Impact%20of%20COVID%20report.v4.pdf?VersionId=apq4P8Je32LhgaQFd0h8HyZ_DMxWw9

7 https://www.muscular dystrophyuk.org/static/s3fs-public/2021-07/PDF-Report-Reaudit-of-unplanned-hospital-admissions-2017.pdf?VersionId=P7yarQ24MjyyMkgJg6_9mg_DeSbT7t2

Newborn screening for spinal muscular atrophy (SMA)

SMA is a rare, genetic neuromuscular condition causing progressive muscle wasting (atrophy) and weakness. Approximately 1 in 10,000 babies are born with SMA. SMA may affect crawling and walking ability, arm, hand, head and neck movement, breathing and swallowing. There are different forms of SMA and a wide spectrum of how severely children and adults are affected. The majority of babies diagnosed with the condition (c. 60%) are classed as having SMA type 1, the most severe form. Without treatment, babies born with this most severe form would see symptoms appearing by 6 months of age and a life expectancy of less than two years, largely due to progressive respiratory deterioration.

There are now three disease modifying treatments available for SMA, all of which have been proven to be effective in arresting the progression of the condition. The efficacy of all three treatments is proven in clinical trials to be strongest if they are administered as early as possible, prior to irreversible motor neurone damage occurring. One treatment, Zolgensma™/ Onasemnogene abeparvovec has been recommended by NICE to be made routinely available via the NHS to the majority of babies with SMA who are diagnosed pre-symptomatically⁸ and two treatments (Spinraza™/ Nusinersen and Evrysdi™/Risdiplam) are available through managed access agreements for pre-symptomatic use.⁹

However, in the absence of the availability of newborn screening for SMA, a child is only diagnosed pre-symptomatically in the UK if they are one of an exceedingly small cohort who are picked up because of a known family history e.g. an affected sibling. The vast majority are not diagnosed until later, and even once symptomatic, families frequently face lengthy diagnostic delays. Children may have to undergo invasive investigations to rule out other conditions as part of the diagnosis process. By relying on symptoms to diagnose SMA, instead of newborn screening, progression of the condition will have occurred, meaning that children live with lifelong significant disability and health complications.

A mother to a child living with SMA gave oral evidence to the inquiry highlighting the challenges for children living with the symptoms of SMA and the impact of babies not receiving treatment until motor neurone damage has occurred:

I think there needs to be a bit more accountability for the ethics of not screening, to be honest. I think there's huge ethical implications of treating after the symptoms have started and you are living with really severe complex needs. It's the health implications. It's the real suffering that comes with it. the Intensive Care admissions, which again, are very, very expensive. I don't think it is really understood the life that these children are having to live, because as families we are seldom asked. This means the cost implications aren't understood as well. My son has had 10 PICU admissions, and none of them were shorter than a month. That's £2,000 per night. He has eight-hour nursing care at school. He has 12-hour nursing care at home. That's a huge amount of money. His school have had to make adaptations. That's a lot of money.

– An advocacy group/patient organisation representative roundtable participant

This example highlights not only the great personal cost to the well-being of a child and their family, but also the related health and social care costs of not detecting and treating SMA at the earliest possible opportunity via newborn screening.

⁸ <https://www.musculardystrophyuk.org/news-blogs-and-stories/news/nice-publishes-new-guidance-for-zolgensma-treatment-in-pre-symptomatic>
⁹ For babies with 1-4 copies of SMN2.

Novartis have carried out analysis which estimates that in the UK, per SMA newborn cohort born in any one year, if the condition was detected and treated pre-symptomatically, over an entire lifetime this would result in a cost saving of £62 million¹⁰.

1.3 Recommendations on how a more pragmatic approach could be developed by the UK NSC

Evidence gathered in the inquiry highlighted several ways in which a more pragmatic approach to assessing conditions for newborn screening could be implemented.

1.3.1 Greater consideration of international evidence

‘National and International Collaboration’ is an underpinning theme of the Rare Disease Framework and Action Plans, highlighting the importance of collaboration given the often-limited evidence and research available around rare conditions. Specifically for newborn screening, the 2022 England Rare Diseases Action Plan states that:

*Opportunities will also be taken to engage internationally and learn from, and contribute to, international best practice on screening.*¹¹

There are a range of conditions that are screened for in newborns internationally that are not currently screened for in the UK. This means that evidence relevant to the assessment of a condition by the UK NSC may already be available internationally, either via established screening programmes or pilots that have been carried out in other countries.

Participants in the inquiry felt that any data that already exists internationally in similar health systems that offer effective, robust national newborn screening programmes should be considered by the UK NSC. This is particularly important considering challenges of evidence generation for rare diseases and would prevent the UK NSC having to replicate work done elsewhere and provide a starting point for assessment. This would play a key role in expediting the assessment process.

It is short-sighted to require UK evidence on screening programme efficacy and not consider the success of screening programmes in other similar health systems

– A clinician who specialises in rare diseases responding to the survey.

The committee tend to take a view that they have to gather the evidence themselves and there is evidence already available through numerous worldwide studies. Why that evidence should differ in the UK population compared to the population of the United States or the population of Germany, I really do not know. That they insist understanding what the incidence is in the UK I think is totally and utterly inappropriate, especially when there is an urgency to move forward

– A clinician who specialises in rare diseases attending the roundtable.

1.3.2 The UK NSC should change the approach to reviewing conditions that have undergone past newborn screening assessments.

Inquiry evidence suggests that lengthy timelines currently involved in the UK NSC assessment process are in part due to the ‘review cycle’ approach taken by the Committee. There are examples of conditions, such as Mucopolysaccharidosis type I (MPS) and Adrenoleukodystrophy (ALD) where,

¹⁰ www.novartis.com/uk-en/news/media-releases/zolgensmav-onasemnogene-abeparvovec-receives-nice-final-draft-guidance-presymptomatic-babies-12-months-spinal-muscular-atrophy-sma

¹¹ https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1057534/England-Rare-Diseases-Action-Plan-2022.pdf p.17

because they were previously considered to be inappropriate for newborn screening, they will not be considered for review again for a number of years.

The National Screening Committee ask for submissions of what conditions to screen for every year. In my experience I submitted for a condition in December 2021. In Autumn 2022 they notified of positively considering it for inclusion in their work program of reviews for 2022 to 23 – but then they are looking at evidence from then, so it will take nearly 18 months for them to actually review. This is because conditions are just put on this year review cycle with no momentum being driven forward by the NSC.

– An advocacy group/patient organisation representative roundtable participant

I'm not sure how it worked but SMA was reviewed in 2018 and seems to be put on a three-year review, which seems very rigid... three years is not agile enough.

– An advocacy group/patient organisation representative interviewee

The implications of the review cycle – spinal muscular atrophy

SMA was reviewed by the UK NSC in 2018 where a decision was made not to recommend it as a condition for newborn screening at that point. Some of the reasons given for the UK NSC decision were¹²:

- there is no evidence for effective treatments for people who do not show symptoms of SMA.
- the long-term effects of a new treatment called nusinersen which can improve symptoms in children with SMA are unknown.
- there is no evidence on the effectiveness of nusinersen in children without symptoms.

SMA was then put onto a review cycle, with plans to re-visit the condition in 2021/22. Yet the year after the 2018 review, in July 2019, the first disease modifying treatment for SMA (nusinersen/ Spinraza) was made available in England, Wales and Northern Ireland via a managed access agreement (MAA). In Scotland nusinersen became available routinely for those diagnosed with SMA type 1 and via the ultra-orphan pathway for all those who have SMA Types 2 or 3. These funding arrangements also offered the opportunity for some babies where there was a family history of SMA to be diagnosed and treated pre-symptomatically¹³. This represented a significant development in changing the outcome for these babies and as such is an advancement which the SMA community feel should have triggered an expedited review.

The announcement of plans to review SMA for newborn screening came in November 2022 and with it a recognition by the UK NSC that there had been significant developments in SMA treatments since the last review in 2018. However, based on prevalence data for SMA, it can be estimated that in the time between nusinersen being made available for pre-symptomatic use in 2019 for babies that met the eligibility criteria (which applied to the majority of babies born with SMA) and the writing of this report, **up to 245 babies and children¹⁴ have developed symptoms of SMA including significant and complex health implications, who could have been treated earlier if newborn screening had been available to coincide with the availability of treatment**, rather than the re-assessment process for SMA not starting until over three years later. This number will further increase whilst the re-assessment is completed.

12 <https://view-health-screening-recommendations.service.gov.uk/sma/>

13 In 2019, the initial nusinersen managed access agreement eligibility criteria for pre-symptomatic treatment was: "immediate access to treatment should be offered with 1 SMN2 copy where Type 0 SMA is not yet apparent. Patients with 2 SMN2 copies will be eligible for treatment. Patients with 3 copies of SMN2 and an older sibling who was diagnosed with type I or II SMA will be eligible for treatment." In January 2022 a variation to the MAA extended the eligibility criteria for pre-symptomatic treatment with nusinersen to include patients with 1-4 SMN2 copies.
<https://www.nice.org.uk/guidance/ta588/resources/managed-access-agreement-july-2019-pdf-6842812573>
<https://www.nice.org.uk/guidance/ta588/resources/variation-2-to-the-managed-access-agreement-pdf-10954550125>

14 <https://www.ncbi.nlm.nih.gov/books/NBK533981/>

Inquiry participants felt that when conditions are reviewed once and then re-assessed at a later date, the process should focus on gap filling, with clarity as to what level of further evidence is required, rather than starting from scratch.

Where a condition has already been reviewed by the NSC, the re-assessment should be a gap filling exercise.

- Survey respondent from charity that work with or on behalf of children and young people with a rare condition

1.3.4 Enhanced horizon scanning is needed to align newborn screening decisions with the availability of treatment for rare conditions.

With the progress made in developing disease-modifying treatments, such as gene therapies, for some rare conditions in recent years, the importance of the UK NSC looking to horizon scanning has increased. Many people in the rare disease community highlighted a potential missed opportunity in terms of horizon scanning for treatments which would impact the assessment of a condition for newborn screening. It was felt that as soon as therapies for a condition are under consideration by health technology assessment bodies, this should automatically ‘trigger’ the process of assessing the appropriateness of newborn screening for that condition. This would require the UK NSC to work closely with health technology assessment bodies across the UK to understand when treatments are expected to be appraised and align their assessment timings. If this approach was taken, then the UK NSC could align their assessments with health technology appraisals so that a rapid decision can be made about newborn screening once a treatment has been approved.

This way of working would be a proactive approach which would ensure there are not situations where therapies are licensed by the Medicines and Healthcare products Regulatory Agency (MHRA) and available via the NHS but may not be achieving optimal outcomes because they are not being administered at the earliest opportunity due to a lack of newborn screening leading to low detection rates. These treatments are instead currently only being delivered at the earliest possible opportunity to babies tested due to having affected family members. This creates not only vast missed opportunity, but also health inequality.

In the case of zolgensma [a treatment for spinal muscular atrophy], there are very few newborns who can be diagnosed pre-symptomatically – which are identified pre-symptomatically via sibling or carrier.

- UK Health Economist

Metachromatic leukodystrophy (MLD)

MLD is a genetic condition that causes severe damage to the affected child’s nervous system and organs, resulting in a life expectancy of between just five and eight years. There is now a disease modifying gene therapy available, Libmeldy, which is funded by the NHS as a specialist service. The first child to receive this treatment was able to do so pre-symptomatically via a sibling related diagnosis. Unfortunately their older sibling was not eligible for the treatment as the clinical guidance requires the gene treatment to be administered before the irreversible damage caused by the condition progresses too far.

Additionally, it was suggested by some, that the UK NSC and health technology assessment bodies could work collaboratively on not only evidence collection about efficacy of a potential treatment, but also potentially on sharing overlapping work which is done by both bodies to determine whether appropriate pathways for the management and treatment of a condition can be identified and understood.

1.3.5 The UK NSC should facilitate more efficient use of newborn screening pilots.

There are several types of pilots of newborn screening that operate in the UK. On the one hand, there are some pilots, on “in service evaluations” that are run by the UK NSC and NHS England to collect additional evidence to enable a positive recommendation of routine newborn screening for a condition, such as the Severe Combined Immunodeficiency (SCID) pilot.¹⁵ Additionally, there are pilots run by others, such as clinicians and universities, to support evidence collection, such as the Thames Valley SMA Pilot¹⁶.

Whilst inquiry participants acknowledged the value of pilots in generating real world evidence on newborn screening, there was also the view that there may be faster and more efficient ways to reach conclusions about newborn screening for rare conditions without setting up individual pilots for a condition each time. For example:

Pilots could consider evaluating several conditions at once where the technology permits, as this could reduce the cost of in-service evaluations – for example machines currently being used for the SCID pilot are also able to test for spinal muscular atrophy.

– Academic / researcher survey respondent

[We] believe that the current criteria demand an excessive number of UK pilots, which delays decision making. Given the availability of data associated with rare diseases, we question the need for the geographical variation of pilots, especially within different nations within the UK. The non-acceptance of evidence from other countries, even when they have similar rigor and health expenditure per capita to the UK, fails to understand the unique challenges in collecting data in rare diseases.

– Pharmaceutical industry survey respondent

Equally, as mentioned in the previous section, similar pilots might also be running, or have previously taken place, in other countries. When this is the case, if it can be determined that the international standard for setting up pilots meets the UK standard, the UK NSC could review the findings of these pilots and therefore potentially expedite the assessment process. The UK NSC could look to form strategic links with certain countries with similar health systems to be able to do this.

Another respondent suggested that if newborn screening pilots were initiated by the UK NSC with the support of clinicians who specialise in the condition being assessed, the aims and objectives of the pilot could be designed in collaboration to fill pre-determined evidence gaps. This would provide additional transparency and would be more efficient and less time consuming than the current situation where third parties are designing pilots to generate evidence that they think the UK NSC are probably looking for. Additionally, it is known in the rare disease community that some voluntary organisations are spending their own money to help drive forward pilots and real-world evidence.

15 <https://phescreening.blog.gov.uk/2021/09/06/evaluation-launch-newborn-scid-screening-nhs/>

16 <https://www.ox.ac.uk/news/2022-03-11-first-uk-pilot-study-newborn-screening-spinal-muscular-atrophy-launched->

Sometimes we see that stakeholders interested in the benefit of newborn screening run their own pilots to try and collect hordes of data which they think they will need to appease the NSC evidence process. This requires a lot of resource and time. Instead, the NSC should instigate pilots with the support of stakeholders to work towards satisfying evidence gaps.

– Clinician specialising in rare conditions.

1.3.6 The current approach that the UK NSC takes to economic modelling should be reviewed.

Inquiry responses highlighted that economic modelling undertaken or commissioned by the UK NSC should be a focused project with ambitious timelines, so as not to delay the overall assessment timelines. The recent guidance published by the UK NSC on the use of economic modelling is welcome because it provides additional clarity and transparency¹⁷. However, the inquiry found that there is also a need to take a more pragmatic approach to modelling as currently the timelines associated with this process are too lengthy, especially when there are often existing metrics and data that can be utilised to reach robust conclusions about the cost effectiveness of newborn screening for certain conditions without starting from scratch.

Tyrosinaemia type 1

The UK NSC has recently recommended screening for tyrosinaemia type 1 in newborns. However, the assessment process has been a lengthy one. One of the inquiry participants highlighted that the UK NSC recommended modelling for tyrosinaemia type 1 in 2017. The final report was not completed until July 2021 and newborn screening for the condition was not recommended by the UK NSC until 2023.

It was further mentioned that the current UK NSC approach to outsourcing bespoke cost effectiveness projects to external institutions means there is a lengthy procurement and delivery process for the final modelling output.

Evidence ‘products’ (e.g., evidence maps, evidence reviews, cost-effectiveness studies) are usually outsourced by the UK NSC to universities or consultancies. Consideration should be given to improving the agility of the external procurement process and the timelines within which providers are expected to complete their work. Examples include (1) ~13 months from the decision to appoint an external provider for the current SMA review to procurement being completed and the University of Sheffield starting work. (2) ~4 years from the decision to commission a model to evaluate the clinical and cost-effectiveness of screening for Tyrosinemia type 1 to the date of the final report by the University of Warwick.

– Academic / researcher survey respondent

A key recommendation to emerge from the inquiry is that the UK NSC should not automatically seek to develop complex models to determine cost effectiveness from scratch. In cases where an economic model relevant to a rare condition has been prepared by others, including members of the appropriate clinical community, this should be taken as a starting point by the UK NSC, prior to commissioning new full-scale models.

One health economist told the inquiry that it was highly likely that distinct groups who have the same research question would come up with models that are very similar – especially as they will be using the same data available from clinical trials.

¹⁷ <https://www.gov.uk/government/publications/uk-nsc-disease-clinical-effectiveness-and-cost-effectiveness-modelling/uk-nsc-disease-clinical-effectiveness-and-cost-effectiveness-modelling#examples-of-models-previously-completed-by-the-uk-nsc>

As a trained UK Health Economist, I will say that if you do the modelling properly - starting with the research question – everything else follows from there: meaning other groups being commissioned to do the modelling who have the same research question and same data available would very likely come up with another model that is very similar. So, it wouldn't make sense to have a new model being created as in the end it would be very similar to ones already done.

– UK Health Economist interviewee

Considering the likelihood of very similar economic models being created by different economists, it seems inefficient to devise a new model from scratch if there are existing models. Instead, the UK NSC and stakeholders should find ways to collaborate and share models and analysis. It is likely that stakeholders are unsure about what the processes and methods of this collaborative approach to modelling would be, so the duty and obligation should be on the UK NSC to drive this forward.

Economic modelling: Severe Combined Immunodeficiency (SCID)

In the case of SCID, it is understood that there were studies demonstrating cost effectiveness of newborn screening available and published in peer reviewed journals, which were presented to the UK NSC. However, the decision was taken by the UK NSC to commission their own cost effectiveness analysis. This took another year to complete, and resulted in the same conclusions that had been published previously.

It is important that where relevant and considered evidence already exists, that there is a strategy for incorporating it into the UK NSC assessment evidence, sharing and adapting for the UK's purpose. This would reduce the need to start from scratch, reducing the workload and, most importantly, hastening the timeline.

– Advocacy group/ patient organisation survey respondent

Chapter 2: Reviewing the criteria and evidence requirements for a condition to be accepted for newborn screening so that they are fit for purpose for rare conditions:

2.1: The rare condition community's perceptions of the current UK NSC criteria and evidence requirements:

Findings from the inquiry supported the importance of the assessment of rare conditions for newborn screening being robust but highlighted that it must also be pragmatic and appropriate for the conditions being assessed.

For rare conditions, the development of a large body of evidence to support newborn screening can be challenging. Evidence requirements from the UK NSC should be proportionate, flexible, and not designed to stand in the way of a positive decision when the overarching case for screening is strong.

– Advocacy group/patient organisation survey respondent

Inquiry participants felt that the current criteria, which must be met for a condition to be recommended for newborn screening, are not compatible with rare diseases. For example, the criteria require an understanding of long-term outcomes of treatments, which may not be known, gathering evidence via randomised control trials, which are often not achievable due to a low population incidence.

The criterion on screening effectiveness calls for evidence from high-quality randomised control trials that the screening programme is effective in reducing morbidity and mortality – this is simply not feasible for rare conditions due to the incident population.

– Advocacy group / patient organisation survey respondent

2.2 Recommendations for developing criteria and evidence requirements that are fit for purpose for rare diseases:

2.2.1 A more flexible approach to evidence requirements is needed.

Inquiry findings suggested the need for a more flexible approach to evidence requirements to be adopted by the UK NSC. Firstly, in terms of the current requirement that a condition must fulfil all the pre-defined criteria for it to be considered for newborn screening, it was highlighted that in the case of rare diseases, it is not realistic to expect all criteria to be fulfilled – as the very nature of the disease being rare is at odds with what is being asked for and required in the criteria. Where there is a broad 'package' of evidence that indicate that newborn screening for a particular condition would be beneficial, there should be appropriate leeway for the UK NSC to make decisions based on the available evidence. Key to this is for the UK NSC to engage with rare condition experts and stakeholders throughout each review process to understand what evidence can feasibly be requested.

Evidence requirements from the UK NSC should be proportionate, flexible, and not designed to stand in the way of a positive decision when the overarching case for screening is strong. For example, where NICE or SMC approved treatment is available and evidence indicates

that diagnosis via newborn screening is clinically and cost effective, NSC committees should be given appropriate leeway to make a decision based on the available evidence. Where uncertainty persists, screening could first be introduced via a national pilot to allow for additional data collection.

– Advocacy group / patient organisation survey respondent

It is right that decisions on population screening are evidence-based, but the quantity and quality of evidence required by the committee may not be achievable for rare diseases, and a more pragmatic approach is needed.

– Academic / researcher survey respondent

We strongly believe that the criteria for newborn screening must be made more flexible in order to effectively cover rare diseases.

– Pharmaceutical company survey respondent

Findings also highlighted the importance of the UK NSC providing greater clarity and transparency as to what evidence is required to satisfy each criterion. Currently the review of a condition for newborn screening is viewed as highly subjective, which makes it hard for clinical and patient communities to understand how they can support the development of appropriate evidence and materials in advance of an assessment by the UK NSC.

2.2.2 The UK NSC evidence requirements should be aligned with other regulators and health technology assessment bodies.

Inquiry participants felt that the UK NSC's approach should be more closely aligned with approaches taken by regulators and health technology assessment bodies to adapt their processes to be more realistic and pragmatic for rare diseases. For example, in 2022 NICE introduced changes as part of its *Methods and Process Review*¹⁸ with the aim of allowing greater flexibility over decisions about value for money and consideration of a broader evidence base. Some of these changes are very relevant for application to UK NSC decision-making. These include:

- Expanding on, and improving, how the organisation considers real-world evidence from the lived experiences of patients, and the value it puts on this experience.
- Allowing more flexibility in decision-making where it is particularly difficult to generate enough evidence, such as considering uncertainty appropriately, and managing the risks to patients and the NHS while preventing inappropriate barriers to valuable innovations.

In the inquiry roundtable discussion, it was noted that the positive impact of these changes has been reflected in recent appraisals by NICE, resulting in more leeway in terms of accepting a small amount of uncertainty around rare conditions. For instance, regarding a recent treatment appraisal for Pompe disease, the final outcome rhetoric was more open-minded about the evidence base.

Recently from NICE we've seen a bit more latitude in terms of accepting a bit of uncertainty around rare conditions in particular. For a treatment for Pompe disease, the final outcome was "we're unclear on the evidence but given the low number of people and the severity of their condition, and the impact it can have on them, we're prepared to be a bit more open minded about the evidence base." I think that's a really welcome approach and one the NSC could warm to

– Advocacy Group roundtable participant.

Equally, the Scottish Medicines Consortium (SMC) was highlighted as an example of proactively working to give patients fairer access to medicines for rare diseases, with a focus on developing a ‘consistent and quick to implement’ process. If the SMC considers an ultra-orphan medicine to be clinically effective, it will be made available on the NHS for at least three years while information on its effectiveness is gathered.

Inquiry participants highlighted the need for enhanced joint working and shared learning between NICE / other health technology assessment bodies and the UK NSC. Patient groups reported that there is often a lot of repetition in terms of engagement and evidence requirements for these bodies and for the UK NSC. Patient groups said that participating in the NICE appraisal process to secure access to a treatment for a condition, only to then have to start another assessment process with the UK NSC to provide similar evidence on the importance of newborn screening for the same condition is frustrating. It provides challenges in terms of the adverse impact of delaying treatment on babies born with one of these conditions and on the resources of patient organisations.

Patients with rare diseases (or their parents), clinical experts, industry and academia invest significant time and effort in supporting the appraisal of medicines and treatments for rare diseases, the development of clinical guidelines, setting up and maintaining disease registries and optimising NHS pathways across the four health systems in the UK. As a matter of principle, the UKNSC should not seek to redo, re-evaluate or in any way duplicate the work already done by other public bodies. To do so places an unreasonable burden on the community and makes UK NSC decision-making inefficient and slow.

– Academic / researcher survey respondent

I believe that NICE is the body that should assess the treatment’s efficacy and the NSC should accept that and not do any further work on that – it’s duplication of effort. They still seem to be wanting to re-do the evidence and I don’t think it’s their job.

– Advocacy group / patient organisation interviewee

Libmeldy for Metachromatic leukodystrophy (MLD)

Taking a recent approval by NICE for the gene therapy for MLD as an example - the patient organisations, clinicians and scientists did a significant amount of work to highlight evidence around the benefits of pre-symptomatic treatment with Libmeldy for babies diagnosed with MLD. This resulted in NICE guidance recommending Libmeldy for MLD. However, despite the treatment being appraised and recommended by NICE, the UK NSC require additional evidence around the importance of pre-symptomatic diagnosis and early treatment of the condition.

2.2.3 The importance of the UK NSC recognising real world evidence when assessing conditions for newborn screening:

Inquiry participants felt the UK NSC must assess other forms of evidence collected outside of clinical trial settings when looking at rare conditions. This approach has increasingly been taken by organisations such as NICE to address uncertainties in clinical trial evidence or when the full reporting period of a clinical trial has not yet completed. When this is the case, in England, Wales and Northern Ireland a treatment may be available via a Managed Access Agreement (MAA) whilst further data is collected. One survey respondent highlighted the importance of including MAAs when the UK NSC are reviewing whether there is effective treatment available for a condition.

A medicine in an MAA has already demonstrated some level of clinical effectiveness... There are also examples in spinal muscular atrophy, whereby multiple medicines are in some form of MAA, therefore the likelihood of failure of all treatments to be routinely commissioned is extremely low.

– Advocacy group / patient group interviewee

It was suggested that the UK NSC should routinely be using real world evidence that has been published in reputable journals.

Chapter 3: Adopting a clear and transparent approach focussed on stakeholder involvement:

3.1 The importance of rare condition stakeholder involvement in the UK NSC review process:

The Rare Diseases Framework and 2022 England Action Plan recognise the importance of the ‘patient voice’. These policies demonstrate a commitment to ‘putting the voice of the rare disease community at the heart of policy-making,’ highlighting that people living with rare conditions, their families, carers, and the organisations that support them have a great amount of knowledge and lived experiences to share.

Due to the limited evidence base available for many rare conditions, advice from condition specialists, people with lived experience and patient organisations should play an even more significant role in enhancing understanding of the suitability of a specific condition for newborn screening.

By leading a collaborative approach with the patient and clinical community, the UK NSC would have a wider perspective, including real world evidence. Stakeholders could work together with the UK NSC to collate and assess evidence, rather than coming to their own conclusions about what kinds of evidence might expedite a decision.

– Advocacy group / patient organisation survey respondent

The rare disease community can offer unique expertise in terms of their lived experience of conditions, ethical considerations, such as the acceptability of the screening test and input into discussions around good versus harm. Condition specialists can provide vital clinical context around conditions, such as care pathways and the clinical importance of prompt diagnosis. Currently it is felt that these opportunities to enhance the evidence base around rare conditions during a review by the UK NSC are not being utilised.

3.2. Perceptions of current approach taken by the UK NSC to stakeholder engagement

The following themes were evident when participants discussed the approaches that the UK NSC takes to stakeholder engagement:

- The onus is very much on the patient organisations and rare disease community to drive efforts for adding a condition to newborn screening and to engage with the UK NSC.
- There has historically been very limited dialogue and engagement between the UK NSC and stakeholder groups throughout the assessment process.
- There is not sufficient transparency around UK NSC processes and evidence requirements to facilitate stakeholder involvement.

It was felt that this indicates that the UK NSC does not place sufficient value on gaining input from stakeholders with condition-specific knowledge. As highlighted by one survey respondent:

Currently the UK NSC receives a submission which is generally made with the collaboration of a rare disease patient organisation, a supporting clinician and with support from the

scientific community. Then the submitters hear very little about what is happening, and information is drip fed to the supporting clinician. There is no engagement with the patient organisation and other stakeholders at the earliest stage. Most engagement is driven by the patient organisation and not by the UK NSC. Engagement usually takes place after the UK NSC has given its decision rather than involving and utilising the expertise and resources of the patient organisations and others in the decision-making process. We are here to help; however, the UK NSC is reluctant to both engage and be transparent about what is happening. We waited many months without any communication.

– Advocacy group/ patient organisation survey respondent

3.3 The UK NSC should take a more proactive approach to identifying conditions for newborn screening.

It was highlighted that in recent cases of conditions being assessed and ultimately accepted for newborn screening, the impetus for this process has come from patient organisations, clinical condition specialists and scientific professionals, instead of from the UK NSC.

The inquiry was told that the responsibility of proposing conditions to add to newborn screening should not be taken on by the rare disease community, but instead the UK NSC should take a proactive role in identifying appropriate conditions and then actively engage with the condition specific community to gather evidence.

The NSC is meant to be a screening committee that is looking for implementation of screening for certain disorders – it should not be for the community to start proposing. Why are they not looking actively for conditions and saying this is the right way to diagnose this condition – they should be proactive and engaging with community to gather evidence. At the moment it is completely reactive. I do think this is about the make-up, the value and mindset and resource that it has. That is their duty of care to the children of this country and they're failing.

– Clinician participating in the roundtable discussion

One example is the experience of the SCID community. The SCID community lobbied through Parliament for the implementation of the newborn screening pilot, which led to the UK NSC engaging with them.

When we wrote the first case for screening for SCID we didn't hear from the committee for months and months and months. Not a word. We actually lobbied through Parliament, and some questions were tabled in Parliament about what is happening. Only after that level of campaigning were we invited to start talking about this process and had we not tabled questions and raised to that level, nothing would have happened. That shouldn't be the case of how you actually start to get the attention of the screening committee.

– Clinician participating in the roundtable discussion

Participants highlighted concern about the level of resource and financial cost required of patient organisations to generate the necessary evidence around newborn screening for the conditions they represent. It was felt that this leads to inequity in the rare disease landscape, with smaller organisations with more limited resources and funding potentially finding themselves disadvantaged in the process.

3.4 There needs to be a greater dialogue between the UK NSC and rare diseases community.

Many stakeholders commented on a lack of communication from the UK NSC during the review process for a condition. For example, in the case of SMA, it is understood that a submission for screening was made in 2018 but there were no meetings or discussions around this submission – only a resulting negative recommendation.

Other patient organisations noted that they were not clearly informed of the timelines for the stages of the review. For instance, they reported working to pull together portfolios of evidence at the request of the UK NSC, only to be told that the resulting outputs would not be considered imminently due to there being no upcoming committee meetings. Participants mentioned that once a committee meeting does take place it is not clear what will happen as a result of the stakeholder evidence, or what the next stages in the review process will be. There were examples of stakeholder evidence being submitted and then the organisations involved not receiving a follow up response for months.

Greater clarity on timelines and expectations for inputs are vital to ensure that stakeholders can prepare for engagements with the UK NSC. Efforts should also be made to understand where different stakeholders can add value and that any requests take into account the demands on their time. For many rare diseases, patient organisations are small and have limited resource, so ensuring that their time is respected and well used is vital.

– Advocacy group / patient organisation survey respondent

There should be a platform for dialogue between the committee and Charities/Research centres that represent the voices of the community of patients where any significant changes (breakthrough developments) could be reported.

– A parent of a person living with a rare condition

Encouragingly, the inquiry also heard that in the case of the most recent review of SMA for newborn screening, which was announced in November 2022, there has been a positive change in terms of the stakeholder engagement undertaken by the UK NSC, with a greater focus on collaboration.

3.5 Overall the UK NSC can learn from stakeholder engagement approaches taken by other organisations.

Improving the approach to stakeholder engagement and recognising the value of the contributions of lived experience representatives is also a focus of other assessment bodies. Whilst as highlighted above, the current UK NSC review of newborn screening for SMA represents an improved approach to working collaboratively with those with expertise of rare conditions, it was felt that the UK NSC could look at collaborative approaches used by other organisations who operate within the rare conditions landscape. Participants in the inquiry highlighted organisations such as NICE and the Scottish Medicines Consortium (SMC) as examples of organisations who had made significant improvements in their approaches to stakeholder engagement.

I feel valued as a patient expert by NICE through the whole process - they really delve deep into our opinions and our thoughts on it. We submit papers beforehand; we are invited to the

meetings. I don't see why the newborn screening committee can't do the same thing.

– A parent of a person living with a rare condition

It's really worth looking at how the Scottish Medicines Consortium are very good at being very clear on what the role of patient groups are and being very clear that it's not for patient groups to have to pull together clinical evidence. They really explicitly talk about hearing lived experience of a condition of the treatment as opposed to sending patient groups off to gather clinical evidence.

– Advocacy group / patient organisation roundtable participant

3.6. Recommendations for improving stakeholder involvement

3.6.1 Stakeholders should be involved at all stages of the assessment process.

Rare condition stakeholders who took part in the inquiry highlighted the importance of being involved early in the assessment process of a condition – at the scoping phase. It was felt that this approach would make the overall review process and the involvement of stakeholders most effective, because as experts in their own field they can signpost UK NSC to evidence that is already available.

In 15 years of advocacy on newborn screening I have never known the NSC to sit down with stakeholders at the outset of a submission ever. Recent moves towards holding expert stakeholder workshops on rare diseases being considered for NBS are very welcome, these help to ensure that our national expertise is brought to bear on the committee's work.

– Advocacy group / patient organisation roundtable participant

Starting each assessment with a stakeholder workshop to understand what evidence is already available should shortcut the time needed for evidence collection teams to conduct their data collection procedures. This type of engagement should become the hallmark of the first phase of a UK NSC assessment.

- Advocacy group / patient organisation survey respondent.

3.6.2 There needs to be a greater degree of transparency in the work done by the UK NSC.

Participants in the inquiry felt that there needs to be greater degree of transparency as to the processes involved in a UK NSC review of a condition for newborn screening. This is essential if the UK NSC are to effectively engage with rare condition stakeholders.

Transparency as to what is involved in each stage of a review and key milestones throughout the process was considered vital to enable stakeholders to be effectively involved. The importance of a timeline was mentioned to increase speed in decisions and accountability of the UK NSC and to manage community expectations in a positive way. It was noted that this practice is commonplace for other organisations. For instance, in the NICE process there are timings of committee meetings and expected end dates for decisions in the public domain. Transparent timelines would also enable patient organisations and other condition experts to plan resources around when they may be able to contribute.

Developing a clear, transparent process that sets out when there are opportunities for stakeholder engagement is highly desirable to remove some of the mystery that exists around UK NSC assessments. Ensuring that clinical and patient stakeholders are consulted at the

scoping stage of any assessment, as well as at appropriate points as the assessment programme progresses, is important. The process should be ambitious in its timelines and there should be a 'stop clock', with performance against agreed timelines monitored and reported.

– Advocacy group / patient organisation survey respondent

As is the case in technology appraisals conducted by NICE and the SMC, key stakeholders should be invited to join the UK NSC panels when conditions are being considered. There are spaces on the UK NSC for public involvement, but they are occupied by people representing the public and not people with condition specific experience. This is reflective of the fact that the remit of the UK NSC is so broad and not specific to newborn screening. The European Medicines Agency (EMA) was highlighted as an example of an organisation with a best practice approach for encouraging stakeholder involvement in this sense, as for every committee making decisions about medicines, there is a voice from a patient advocacy group – which should be replicated by the UK NSC.

Appendix

Named contributors to the inquiry:

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All Party Parliamentary Group for Muscular Dystrophy

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