UK National Screening Committee

# Review of need for an in-service evaluation for newborn screening for spinal muscular atrophy

**UK National Screening Committee (UK NSC)**
**26 June 2025**

## Purpose

The National Institute for Health and Care Research (NIHR) commissioning brief for the in-service evaluation (ISE) for newborn screening for spinal muscular atrophy (SMA) was developed in Summer 2024 and gained sign off from NIHR in September 2024. Following the cost effectiveness modelling work produced by the Sheffield Centre for Health and Related Research (ScHARR) in early 2025, a review took place to consider whether the research questions of the ISE brief were still relevant and if an ISE was still required. The conclusion was that an ISE is still required. This document describes the analysis.

The NIHR research call was published on 28 May 2025: Spinal muscular atrophy screening | NIHR.

## Review

The ISE research question is: 'What is the feasibility, acceptability, effectiveness, and cost-effectiveness of newborn screening for spinal muscular atrophy (SMA)?'

### Feasibility

This question can only be properly understood through implementation in live screening services to assess screening programme performance and impact. The ISE will test the optimum clinical pathway and test methodology within the context of a nationally delivered newborn blood spot programme in the NHS, ensuring safe movement of babies through the screening pathway. This includes the logistics of administering a programme that is delivered consistently by multiple geographically separated and commissioned screening and genetics laboratories, treatment referral centres and IT systems, including establishing sustainable data collection systems for longer term outcomes. It is expected that the operational feasibility of screening can be assessed within the first year of screening, allowing an interim UK NSC decision to be made on how/whether to continue screening.

### Acceptability

Work is required to understand the acceptability and experience of families of screened babies and the healthcare professionals involved in the screening pathway, for example

regarding the timing and mode of delivery of results. This will support future decision making on the optimal screening pathway, such as when to have SMN2 copy number results available, and whether to disclose results for types of SMA with 5 or more SMN2 copy numbers.

## Effectiveness

Screening for SMA aims to screen, diagnose and treat babies before they have symptoms. The ISE will evaluate the timescales that can be met in UK services at important stages of the screening pathway such as result availability, clinical referral and start of any treatment.

The performance of SMA tests in an NHS environment needs to be evaluated to assure the screening programme of test characteristics (accuracy, reproducibility, resilience and operational utility) and the resulting sensitivity, specificity, positive and negative predictive values of testing.

As the drugs are quite new there is limited research on the clinical effectiveness of treating presymptomatic babies (particularly for risdiplam), so evaluating this within the context of the NHS Newborn Blood Spot Screening Programme is important. Gaining more data on short-term outcomes will contribute evidence as to how clinically effective screening in the UK is.

As long-term effectiveness of novel treatments is currently unknown, the ISE will allow sustainable longer term health outcome monitoring systems to be established, providing an essential capability for assessing the effectiveness of the screening programme. This includes health states, quality of life, mortality and psychosocial outcomes.

## Cost-effectiveness

Although ScHARR's economic model estimates that SMA screening in the UK is likely to be cost-saving or cost-effective, it caveats that there are important uncertainties that could affect the accuracy and conclusions of the model. The ISE will therefore identify further information to allow both clinical and cost-effectiveness to be assessed, using real world UK data. This includes:

- costs involved in screening (including healthcare costs for different health states)
- clinical effectiveness of presymptomatic and symptomatic treatment and the impact of diagnostic delay on presymptomatic babies
- long-term effectiveness of treatment
- how accurate the screening tests are (sensitivity and specificity)
- which treatments patients receive based on their SMN2 copy numbers and how effective these treatments are
- incidence of SMA in UK (types of SMA and SMN2 copies)

## Analysis to support UK NSC recommendation

The data collected within the ISE will be available at different timescales.

For example, short-term outcomes (1 year):

- feasibility outcomes
- the number of cases detected pre-symptomatically
- proportions of the different SMA types (for those detected symptomatically) and SMN2 copy numbers (for those detected pre-symptomatically)
- proportions of patients receiving the different treatments
- having systems in place to allow collection of data on effectiveness of screening and treatment

Mid-term and long-term outcomes (time points defined by NIHR research team and UK NSC):

- further data on the short-term outcomes plus
- effectiveness of treatment in terms of the motor function milestones/ health state
- experience and acceptability outcomes