

# UK National Screening Committee consultation on newborn screening for Severe Combined Immunodeficiency Disorder (SCID)

## British Society of Immunology Clinical Immunology Professional Network (BSI-CIPN) response

*November 2025*

### Summary of Recommendations

- Although not cost effective, the SCID newborn screening programme has been found to be extremely clinically effective. The full economic cost-effectiveness of the programme is likely to have been underestimated (see below), and with adaptations to the screening protocol could be improved. **Terminating the newborn screening programme for SCID would be a significant retrograde step in clinical management and a severe blow to the immunodeficiency community.**
- If combined with SMA newborn screening then it is likely that screening for both diseases will become cost-effective, and we would recommend continuing the SCID newborn screening programme until evaluation of SMA screening is complete.
- We recommend extending screening to the whole of the UK, as the current geographical inequity of care is an ethical and prejudicial.
- We welcome a review of the genetic testing support for the SCID newborn screening programme. We have concerns about referring patients directly for genetic testing without flow cytometry testing as this will increase the risk of missing significant immunodeficiency diagnoses which could result in avoidable death or morbidity. **Any adoption of reflex genetic testing should be carefully risk assessed and should be subject to careful ongoing audit.**
- We support the long term follow up of true positive patients from the newborn screening in-service evaluation as this will give invaluable clinical and health economic outcome data on the true benefits of screening.
- We agree with the need for additional work on parent information and newborn screening counselling to reduce the impact of false positive screening tests.
- We agree with combining monitoring of the BCG vaccination programme with the SCID newborn screening programme as these are inexorably linked.
- We support the standardisation of expert consensus clinical algorithms for the management of non-SCID T-cell lymphopenia, and would support the long-term follow-up of this important cohort of patients.

## Clinical effectiveness

The in-service evaluation clearly demonstrates a marked clinical effectiveness of SCID newborn screening with 92% survival for SCID babies diagnosed through the newborn screening programme compared to 20% in the clinical presentation cohort.

Many patients incidentally diagnosed with non SCID T-cell lymphopenia had already gained benefit from newborn diagnosis. The full clinical and economic benefits for this cohort of patients will only be fully appreciated in decades time. We know that patients who present clinically with non-SCID T-cell lymphopenia disorders usually already have established end-organ damage and lifelong significant health needs. Early diagnosis offers an opportunity to improve clinical outcome in these patients and reduce their high health economic burden.

## SCID newborn screening was welcomed by all parents

Despite the problems with the test's low positive predictive, high numbers of false positives and the distressed caused by false positive results, parents and healthcare professionals have all been highly supportive of the screening program.

## Observations on epidemiology during in-service evaluation

Data generated during the in-service evaluation of SCID newborn screening pilot, illustrates the complexity and pitfalls of population studies in rare diseases. Despite an evaluation period of 2.5 years the birth prevalence of SCID during this period was 1 in 71000, despite a historical UK prevalence of 1 in 53000, and a prevalence of 1 in 33000 in the 12 months following the pilot study. Most European countries and the US where newborn screening has been implemented, have reported a SCID prevalence of between 1 in 50000 and 1 in 60000.

Furthermore, 30% of the SCID babies diagnosed through newborn screening had a recently identified genetic defect (first published during in-service evaluation) or remained genetically undefined. This is far higher than that seen in published cohorts where approximately 85% of SCID babies having "typical" SCID genetic defects. The definitive treatment outcomes (and therefore healthcare costs) associated with these novel disorders are likely to be more unpredictable and higher.

The results from the in-service evaluation illustrate the vast random variability of rare disease year on year prevalence. This introduces potential inaccuracies in extrapolating this data to longer term service evaluation. The cost effectiveness evaluation highlighted that the cost effectiveness of SCID screening markedly improved at higher disease prevalence, and this combined with the atypical diagnoses made by the screening programme is likely to have negatively impacted on the cost effectiveness of the screening programme.

## Quality of life analysis and full economic cost of screening

The economic analysis of newborn screening for SCID has still only been assessed over a relatively short period of time. As clinicians looking after generations of families who have lost 1 or more baby with SCID, we would suggest the full economic impact of a SCID baby's death is underestimated in this analysis. Because of the highly traumatic and psychologically disturbed journey a family has to endure following a clinical diagnosis of SCID (> 6 months inpatient hospital stay, large distances from the family home, prolonged stays on PICU, communication barriers due to language issues, prolonged and distressing deaths), it is very common to see families affected by long term mental health problems, self harming, suicide and attachment/relationship issues with other siblings. This represents a large but hidden economic burden of these diseases.

Within the cost effectiveness report, the QALY dis-benefit of parents receiving false positive results outweighs the QALY benefit of the bereavements avoided through newborn screening. The report also highlights that almost all parents were not aware that SCID was being screened for. Improvements in the perinatal newborn screening counselling and the information provided for parents would reduce the QALY dis-benefit of false-positive results, and re balance the QALY benefit analysis.

## Full economic benefits of SCID newborn screening

The in-service evaluation performed provided an incomparable and exhaustively detailed comparison of 3 diagnostic platforms and a variety of diagnostic threshold cut offs. This has provided a detailed description of strengths and weaknesses of the screening options available but delivering newborn screening in this setting is more expensive than any real-world diagnostic which would be adopted for a substantive program.

Over the long term, cost savings for SCID newborn screening could be achieved by;

- Using tighter positive cut off thresholds or adopting an alternative strategy for premature babies to reduce the number of false positive results.
- Adoption of a single national platform will result in efficiency savings and more efficient trouble shooting for operational problems.
- The cost of SCID newborn screening will reduce over time.
- Given the novel nature of TREC screening (PCR) based, this programme has a higher up-front infrastructure cost associated with it. This infrastructure is likely to be shared with other screening programmes in the future.

Overall, these factors and those discussed in the epidemiology and quality of life comments suggest that SCID screening is likely to be significantly more cost effective than the in-service evaluation suggests in a real world setting over the longer time period.

## Genetic testing

Having clear guidelines as to which patients with positive newborn screening tests are referred for genetics would be highly beneficial and would make ongoing evaluation of the newborn screening programme more robust.

Having appropriate funding and support for a rapid genetic test covering a discrete panel of SCID genes would reduce delays in confirming a diagnosis and delivering definitive treatment. The

current turn around time of 3 weeks for a whole exome sequence based gene panel, results in delayed treatment and is slower than most other leading European countries. An urgent turn-around test could be combined with genetic investigation for the other immunological emergency, primary haemophagocytic lymphohistiocytosis. Genetic testing with a 1 week turnaround for these to disorders would significantly improve clinical care and outcome.

Proceeding to reflex genetic testing without flow cytometry for patients with TREC levels on newborn screening which fall below the threshold cut off but are not absent, may reduce the workload of specialist immunology referral centres, but runs the risk of delaying the diagnosis of a serious immunodeficiency, and therefore delaying the instigation of prophylactic treatment. We know there will always be a significant proportion of babies with serious immunodeficiencies who remained genetically undefined, and without performing flow cytometry on these babies they may be lost to follow-up, only presenting critically ill at a later time point.

## Inequity of current screening situation

Continuing the SCID newborn screening programme in the current format, would result in a post code lottery of survival for babies born with SCID. This geographical inequity of care is unethical and could potentially lead to a legal challenge by a judicial review.

Babies with SCID are disproportionately represented among ethnic minority and families from low socio-economic backgrounds, and therefore termination of the SCID programme would disproportionately disadvantage these patient groups.

## International profile

No other country in the world has initiated a national SCID newborn screening program and then terminated the programme. This decision would leave the UK as an outlier in the management of babies with inborn errors of immunity. Reputationally this would significantly damage the reputation of the UK as a leader in the field of inborn errors of immunity and may reduce international investment in research and research collaboration.

Such a decision may also be at risk of challenge through a judicial review from individual patients or patient groups.