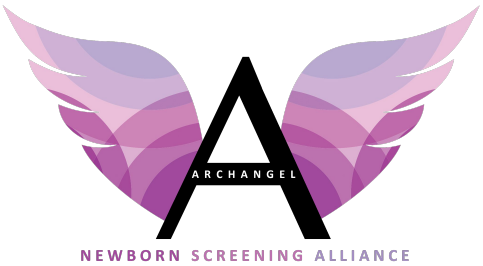


ARCHANGEL NEWBORN SCREENING REVIEW CAMPAIGN & KEY POLICY CHANGES

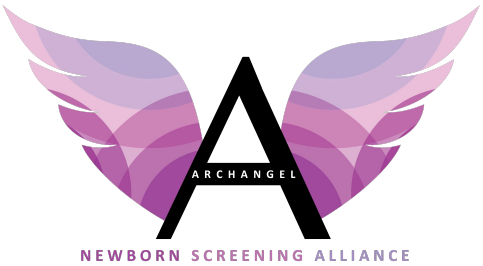
The ArchAngel Newborn Screening Alliance is a multi-stakeholder advocacy group currently comprising 13 principal rare disease patient organisations*, who collectively represent over 500 rare diseases and thousands of patients. A campaign calling for urgent expansion of the UK NBS programme was devised by the group in 2020 in collaboration with Nickie Aiken MP and a number of leading UK scientists and rare disease clinicians. It is supported by Genetic Alliance UK and over 100 cross-party MPs and members of the House of Lords.

Rare Diseases disproportionally affect children and diagnostic delays result in unnecessary suffering and undue burden on the health service. Newborn screening has the power to dramatically improve children's lives, by facilitating early access to treatment, maximising the chance for eligibility for treatments and reducing the chance for serious effects of disease prior to treatment.

Unfortunately the UK Newborn Screening Programme is lagging behind that of many other high-income countries. Inefficient and outdated processes and bureaucracy are failing to keep pace with rapid developments in science and technology and result in significant inequity to our children. The UK system requires urgent revision in order to harness the potential of cutting-edge advances in science and technology, such as Genomic screening and gene therapies, and to guarantee equality of health outcomes for all.

The Rare Disease Framework now gives us the opportunity to make a number of key policy changes which would allow for the appropriate and efficient expansion of the NBS programme.

The following proposed key policy changes have been developed by the stakeholder group in direct response to the Rare Disease Framework commitment to Priority 1: 'helping patients get a final diagnosis faster', with specific regard to Newborn Screening:



1. **BY THE END OF 2022, FORMATION OF A DEDICATED TEAM OF NEWBORN SCREENING EXPERTS TO SOLELY EVALUATE CONDITIONS TO BE ADDED TO THE NEWBORN SCREENING PROGRAMME AND TO UNDERTAKE THE FORMAL ENGAGEMENT OF CONSULTEES, INCLUDING CLINCIAL AND SCIENTIFIC EXPERTS RELEVANT TO THE CONDITION/GROUP OF CONDITIONS BEING APPRAISED**
2. **BY THE END OF 2022, ESTABLISHMENT OF A STREAMLINED EVIDENCE REVIEW PROCESS FOR EVALUATION OF CONDITIONS TO BE ADDED TO THE UK NEWBORN SCREENING PROGRAMME, WHICH IS RELEVANT TO RARE DISEASES AND AUTOMATICALLY ACCEPTS A WIDE RANGE OF EVIDENCE CURRENTLY AVAILABLE FROM VALIDATED AND REPUTABLE SOURCES**
3. **BY THE END OF 2022, THE PROCESS OF EVALUATION OF ADDING CONDITONS TO THE UK NEWBORN SCREENING PROGRAMME TO INCORPORATE SPECIFIED TIMESCALES IN ORDER TO ENSURE APPROPRIATE EFFICIENCY AND ACCOUNTABILITY**

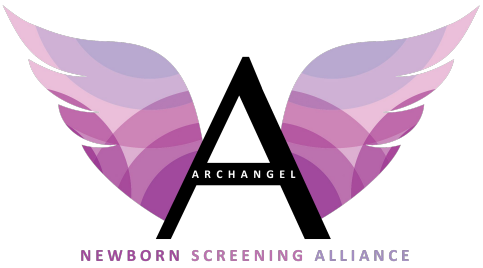
POLICY CHANGE 1.

BY THE END OF 2022, FORMATION OF A DEDICATED TEAM OF NEWBORN SCREENING EXPERTS TO SOLELY EVALUATE CONDITIONS TO BE ADDED TO THE NEWBORN SCREENING PROGRAMME AND TO UNDERTAKE THE FORMAL ENGAGEMENT OF CONSULTEES, INCLUDING CLINCIAL AND SCIENTIFIC EXPERTS RELEVANT TO THE CONDITION/GROUP OF CONDITIONS BEING APPRAISED

- The National Screening Committee (NSC) infrastructure and programme resources are inadequate to enable fair and efficient considerations across all population screening programmes. Newborn Screening is therefore unintentionally discriminated against as programmes applicable to wider sections of the population,

e.g. cancer, heart conditions, are prioritised. In addition to pressure on the system to evaluate new screening programmes, there is also a significant 'legacy list' of previous applications which requires regular review. A dedicated Newborn Screening Team would remove newborn screening from the both the lengthy processing 'queue' and an unfair, unfavourable position in the hierarchy of wider screening programmes.

- Current NSC infrastructure is woefully ill-equipped to meet the demands of constant progress in diagnostic technology and treatments, including Genomics and gene therapies. The advent of opportunities for Genomic screening at birth will significantly increase the number of conditions potentially identified. However, many conditions identified in a first-tier screen may not have potential for secondary testing and/or treatment options. Genomic screening will thus significantly increase the demand for NSC consideration of ethics, validation of new pathways for treatment and case management. The system is already lacking the required bandwidth to fully support the current programmes and will not have the capability to support a burgeoning slate. Baroness Blackwood (Chair, Genomics England) is in full agreement.
- Whilst ground-breaking developments in Genomic screening are welcomed, important and laudable, it is essential to recognise the timing and limits of potential Genomic screening for all children at birth. Scientists estimate that functional genomic newborn screening is many years away and at that point it is unlikely to be viable as a first-tier screen for many conditions, for which it will only have potential as additional or confirmatory screening. There is a clear duty of care not to neglect the conditions which could technically be added to the NBS programme now and those for which Genomic screening will not replace biochemical screening in the longer term.



- An expanded NBS programme would provide numerous benefits to society and the health system. Benefits include: avoiding serious delays in diagnosis currently experienced by many rare disease patients, thereby saving scarce healthcare resources through controlled condition management; improving outcomes for patients by allowing effective and often time-critical intervention; reducing the burden of interaction with and reliance on health services for patients; allowing families the ability to make informed reproductive choices.
- A more comprehensive newborn screening programme would reduce the number of people who are extremely clinically vulnerable to new infectious disease outbreaks/future pandemics.
- There are currently very few experts on Rare Diseases advising the NSC or involved in the detail of the evaluation process. There is no Public and Patient Voice (PPV) member representing the rare disease patient community.
- Evidence reviews are currently commissioned and undertaken by external groups who are considered experts in review methods and research, not in the conditions under consideration. Paediatric and other experts from specialist centres who treat children affected by specific conditions would be well qualified to judge evidence and ensure more equitable and robust decision- making. There is a real opportunity for change.
- The focus on decision making in the UK in terms of giving more credence to the 'harm' that screening might do, rather than the 'good' of saving children's lives is out of balance. More emphasis - without evidence to justify this position - is placed on the possible harm that screening could do to a new family if a baby does not then need treatment, rather than the value of bringing treatment to a child with a previously undetected disease and potentially saving a life. The Rights of the Child are not being given balanced consideration. Experts from specialist centres who treat children affected by specific conditions would ensure appropriate and more

equitable judgment of Harm Vs Good. A true measure of public opinion on the harm of false positives is also long overdue.

POLICY CHANGE 2.

BY END OF 2022, ESTABLISHMENT OF A STREAMLINED EVIDENCE REVIEW PROCESS FOR EVALUATION OF CONDITIONS TO BE ADDED TO THE UK NEWBORN SCREENING PROGRAMME, WHICH IS RELEVANT TO RARE DISEASES AND AUTOMATICALLY ACCEPTS A WIDE RANGE OF EVIDENCE CURRENTLY AVAILABLE FROM VALIDATED AND REPUTABLE SOURCES

- Unrealistic evidence parameters are responsible for lengthy delays and a quagmire of decision making.
- Evidence requirements (e.g. long term outcomes of treatment) for wider population screening programmes are generally not appropriate to rare diseases in children. It is a contradiction to question the efficacy of treatment if the treatment in question has already received approval by the European Medicines Agency (EMA) and NICE, especially in treatments which have proven increased efficacy in cases of earlier intervention.
- Evidence restrictions (e.g. only concerning the UK population; articles not published in English), are too restrictive for rare diseases which have very small populations. Unpublished or 'grey' evidence from relevant and reputable sources (e.g. other countries programmes) is rarely considered. The viewpoint that the UK NSC has to generate evidence themselves is unjustified and can waste years gathering the same data to reach the same conclusion as other studies.
- Current process entails unnecessary duplication of gathering and checking evidence already validated by other relevant and reputable bodies, e.g. NICE, which dismisses the lengthy and costly process of endorsement to PHE on a number of aspects, including understanding of the condition and efficacy of the relevant treatment.

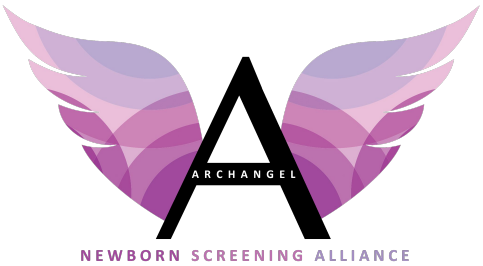
Automatic inclusion of these sources would save valuable time for children, ease pressure on the workload and save revenue which could be redirected elsewhere.

- The UK NSC will only re-evaluate a previously rejected condition after 3 years and reviews are carried out without proper and full consultation, e.g. key stakeholders not being invited to comment. This wastes precious time for patients, especially when new diagnostic methods are validated and treatments are approved for NHS use. Current infrastructure does not allow for the NSC to meet their purported commitment to 'rapid review' of a condition even if new evidence is conveyed.

POLICY CHANGE 3

BY END OF 2022, THE PROCESS OF EVALUATION OF ADDING CONDITONS TO THE UK NEWBORN SCREENING PROGRAMME TO INCORPORATE SPECIFIED TIMESCALES IN ORDER TO ENSURE APPROPRIATE EFFICIENCY AND ACCOUNTABILITY

- There is currently no timescale for evaluation in place, resulting in a process which is inconsistent, fluid and unacceptability protracted. Children have died unnecessarily from lack of access to life-changing treatments due to delayed diagnosis, which could have been prevented by more efficient evaluation of the condition being added to the newborn screening programme. This includes patients with SCID, which has been in the evaluation process for over 10 years (since October 2011), during which time 15 other countries have implemented a screening programme and a further 7 countries have commenced a pilot, with many lives saved.
- Prolonged evaluations are already resulting in a failure to keep pace with advances in science and technology. The increasing velocity of developments such as Genomic screening and gene therapies threaten to render the current system entirely dysfunctional unless an appropriate and accountable timeframe for evaluation is established. The UK is currently regarded as a world leader in Genomics, however that status could be quickly lost if our system is unable to support its developments.



- The current triage process is too vague and slow. Conditions which meet the WHO criteria of a proven test kit and treatment and/or have an existing screening programme in another country could potentially begin the assessment process at current NSC Step 3 on day 1, thereby eliminating excessive bureaucracy and unnecessary delay.
- The NSC is out of step with other public health decision making bodies and there is currently no accountability in the decision-making process. Evidence reviews are not carried out using standardised methodology and there is no quality control of this process.
- NSC and sub-group meetings are not open to the public or stakeholder groups, who have no opportunity to comment on the evidence or the interpretation of evidence, or to resolve any uncertainties.
- Arbitrary workshops held with the NSC further to pressure from stakeholder groups have proven instrumental in breaking an impasse in past evaluations, thus emphasising the need for more formalised stakeholder involvement.
- There is no process of appeal, other than through judicial review, which can only challenge the adherence to process, not the inequity or failures of the process itself.

Further problems with the current system have been identified, including around funding for economic evaluations and early commissioning of proof of concepts studies, however the above key policy changes have been developed to address the most fundamental issues and achieve the most productive change for all relevant conditions. The changes are supported by Lord Bethell, who has described them as “well thought-out, justified and realistic”.

*ArchAngel Newborn Screening Alliance Members: AGSD UK, ALEX The Leukodystrophy Charity, ArchAngel MLD Trust, Battens Disease Family Association, CATS Foundation, Gaucher Alliance, Metabolic Support UK, MLD Support Association UK, The MPS Society, Muscular Dystrophy UK, Nieman-Pick UK, Pompe Support UK, SMA UK.