GENETIC ALLIANCE UK

TIME TO DECIDE

Learning from international approaches to newborn screening decision-making

About Genetic Alliance UK

Genetic Alliance UK is an alliance of over 200 charities and support groups working together to improve the lives of people in the UK with lifelong and complex genetic, rare and undiagnosed conditions.

We advocate for fast and accurate diagnosis, good quality care and access to the best treatments. We actively support progress in research and engage with decision makers and the public about the challenges faced by our community. We run two long standing projects:

Rare Disease UK: A campaign focused on making sure the UK Rare Diseases Framework is as successful as possible, and to ensure that people and families living with rare conditions have access to a final diagnosis, coordinated care and specialist care and treatment.

SWAN UK: The only dedicated support network in the UK for families affected by a syndrome without a name – a genetic condition so rare it often remains undiagnosed.

Contributors

The role of the following country and regional experts in newborn screening has been invaluable in supporting delivery of this report. We are deeply appreciative of this voluntary support and would like to thank the following for their time.

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We would also like to thank the members of:

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- The UK Newborn Screening Collaborative
- EURORDIS Newborn Screening Working Group
- The International Consortium on Newborn Sequencing (ICoNS)

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Our involvement in newborn screening initiatives
Genetic Alliance UK's Chief Executive is a member of the UK National Screening Committee's Blood Spot Task Group (BSTG) and is on the Partnership Board for an in-service evaluation (ISE) for spinal muscular atrophy. Genetic Alliance UK received funding from Genomics England for its input on the development of the Generation Study and is part of the research consortium delivering the independent evaluation. Genetic Alliance UK is a member of the UK Newborn Screening Collaborative. Internationally, our team are also members of the EURORDIS-Rare Diseases Europe Newborn Screening Working Group, the Patient Advisory Board and the Newborn Screening Forum for the EU project Screen4Care, the International Consortium on Newborn Sequencing (ICoNS) and the International Society for Neonatal Screening (ISNS).

Foreword

Newborn screening saves lives and improves outcomes for babies with rare conditions. For the nine conditions currently screened for using the heel prick test in the UK, the programme has transformed how we deliver care, support families, and facilitate research and innovation. This life-changing potential is why newborn screening remains a top priority for people living with genetic, rare and undiagnosed conditions.

In 2019, Genetic Alliance UK published ***Fixing the present, building for the future***, delivering two key messages from our community: that the UK screened for fewer conditions than most European nations, and that it was uniquely placed, as a global leader in genomics, to consider the future of genomic newborn screening. The launch of Genomics England's Generation Study was an encouraging response to that future-facing call. While we do not prejudge the outcomes of the study, its ambition – screening for over 200 conditions – is a cause for optimism.

Since then, we have welcomed the UK Government's recent commitment to offer whole genome sequencing to all newborns by 2035. This bold ambition has the potential to transform early diagnosis and treatment for thousands of children. However, critical questions remain unanswered: which conditions will be screened for, how will they be selected and what role will conventional screening continue to play?

The UK still lags behind most comparable nations in terms of conventional screening. The six years since our report have seen no increase in the number of conditions screened for in the UK. A recommendation to add one additional condition was made in 2022 by the UK National Screening Committee, but implementation is incomplete. In contrast, EU countries recommend screening for an average of 19 conditions (mean 18.6, median 21), and at least 19 of them screen for more conditions than the UK. Australia, Canada, New Zealand, the US and Ukraine also recommend screening for more conditions than the UK.

Of course, no two health systems are identical. But there is a growing international consensus that newborn screening – even without genome sequencing – can and should be used to detect more rare conditions. Before the UK can lead, we must catch up. The lack of progress to date suggests that our decision-making processes may not be fit to deliver the Government's vision for transformational change.

In the UK, a rare condition affects fewer than

1 in 2000 people

3.5+ million people in the UK

are living with a rare condition

If we are to meet the 2035 goal, we need to start building the path now. This report explores how other countries have expanded their newborn screening programmes, and what we can learn from them. To all our genetic, rare and undiagnosed communities who have been refused screening programmes that are offered elsewhere in the world, ten years will be a long time to wait. This report sets out pragmatic opportunities to bridge that gap.

We hope this marks a turning point. It's time for the UK to match its ambitions in rare disease leadership with a clear pathway to faster, smarter decisions in newborn screening, bringing life-changing benefits to more families, sooner.

Nick Meade, Chief Executive, Genetic Alliance UK

1 in 17 people

will be affected by a rare condition during their lifetime

Executive summary

This report was prepared in parallel to the NHS 10-Year Plan for England and written prior to its publication.

1 Evidence

Address constraints on reviewing rare conditions

Use a pragmatic evidence threshold when natural history data is limited.

Avoid duplicating real-world evidence from other countries.

Establish distinct review pathways for different categories of condition.

Drive progress by closing evidence gaps between formal reviews.

Commit to a shorter review cycle where the need is urgent.

2 Partnership

Leverage the expertise of the rare community

Remove barriers to stakeholder participation.

Embed representation of people with rare conditions in all decision-making processes.

Partner with patient organisations to support timely implementation.

3 Transparency

Ensure clarity in decision-making

Adopt an objective scoring framework to strengthen trust in review outcomes.

Publish materials to clarify how screening decisions were made.

Provide regular updates on the status of reviews and initiatives to manage expectations.

Improve accessibility by co-producing materials with patient organisations.

4 Efficiency

Adopt an agile decision-making process

Take a proactive, opportunity-based approach to nominating conditions.

Decouple reviews of clinical evidence from decisions on implementation.

Prepare for new technologies expected to transform screening programmes.

Ensure consistent, equitable access to newborn screening.

5 Innovation

Embed newborn screening into health systems

Establish a pathway to ensure cross-sector collaboration.

Support UK leadership to maximise the opportunities that newborn screening offers.

Case studies are spread across the report and cover a range of learnings.

Please see page 31 for a glossary of acronyms and abbreviations used in this report.

Why is detecting and diagnosing rare conditions early important?

For children with rare conditions, delays to diagnosis can result in severe disability or even death. Rare and genetic diseases ('rare conditions'), disproportionately affect children.[1] Some children can benefit from treatments or interventions, including preventive measures, that are most effective when given before symptoms emerge – and in some cases, before irreversible harm occurs.[2-45] A lengthy 'diagnostic odyssey' for rare conditions is widely known to reduce quality of life for these children and their families.[5-7]

There are several routes to detect genetic and rare conditions earlier, including during pregnancy (prenatal screening) and newborn screening. Screening is a tool to help identify people who are at higher risk of developing a condition before signs or symptoms show.[8] If a person's screening result is positive, they may be referred for further tests before a diagnosis is made. Newborn screening has been a cornerstone of early detection since the 1960s and every baby born in the UK is offered newborn blood spot screening. Also known as the heel prick or Guthrie test, it involves taking a single blood sample to biochemically test for nine rare but serious health conditions in the NHS Newborn Blood Spot Screening Programme.[9] For two of these conditions, genetic tests are carried out as a 'second-tier' confirmatory step before parents are contacted for follow-up.

People living with rare conditions experience a significant health burden. Recent survey data shows 8 in 10 people in the UK with rare conditions have a disability, and most live with more than one.[10] Over half the people surveyed also report experiencing discrimination when accessing essential services. Since 95% of rare conditions currently have no cure, screening programmes can raise awareness and better inform the allocation of health services, thus offering people living with rare conditions a vital first step towards a more equitable means to 'live well'.[11] While most babies screened will not be affected by rare conditions, early detection could dramatically improve health outcomes for those that are.

The NHS currently screens newborns for 9 rare conditions:

- cystic fibrosis
- sickle cell disease (SCD)
- congenital hypothyroidism
- phenylketonuria (PKU)
- medium-chain acyl-CoA dehydrogenase deficiency (MCADD)
- maple syrup urine disease (MSUD)
- isovaleric acidaemia (IVA)
- glutaric aciduria type 1 (GA1)
- homocystinuria (HCU)

Why is the concept of actionability so important to the rare community?

Treatable conditions are those with available clinical interventions that may address symptoms or prevent irreversible harm. *Actionable* goes further: even without a clinical intervention, early diagnosis can improve outcomes by avoiding children needing to undergo a lengthy diagnostic investigation, enabling parents to access support earlier and make informed decisions on their child's care and any future pregnancies.[12-14] An example of a clear non-treatment action is teaching parents and carers how to hold their baby to avoid bone breaks.[15] The majority of the genetic and rare community* is in favour of recognising that some rare conditions are 'actionable' to ensure the wider benefits of screening are also given consideration by decision-makers.[7]

**For brevity throughout this report, 'rare community' refers to the genetic and rare community.*

Who makes decisions on which rare conditions the UK screens for?

The UK National Screening Committee (UK NSC) is a four nations group that makes decisions on whether to recommend newborn screening for a rare condition. The UK NSC is an advisory body appointed by the Department of Health and Social Care (DHSC) that reports to ministers. The UK NSC workplan is developed in agreement with the Chief Medical Officers of all four nations and is supported by a secretariat housed within the DHSC. Recommendations for newborn screening are informed by the UK NSC's Fetal, Maternal and Child Health (FMCH) reference group, which reviews conditions that are nominated for inclusion against 20 set criteria for screening programmes.[16-18]

In Wales, Scotland and Northern Ireland, the UK NSC's recommendations are adopted through devolved decision-making structures tailored to each nation's healthcare system.[18] However, since the process at the devolved level is essentially paused until a positive recommendation from the UK NSC is made (a 'stage-gated' process), it results in a situation where the UK NSC is the de facto decision-maker for newborn screening in the UK.

How the UK makes decisions on newborn screening (a stage-gated process)

	England	Wales	Scotland	Northern Ireland
1 A positive recommendation is made by the UK NSC				
2 Proposes evidence review	N/A *(UK NSC before stage 1)*	Welsh Screening Committee (WSC)	Scotland NSC or the National Screening Oversight Board	Public Health Agency Northern Ireland (PHA NI) *(or advisory committee)*
3 Reviews evidence	N/A *(UK NSC before stage 1)*	Public Health Wales	Public Health Scotland *(may commission another group)*	PHA NI
4 Recommends to implement	NHS England (NHSE) Board or DHSC	WSC	Scotland NSC or Health Improvement Scotland	PHA NI
5 Approves implementation	Secretary of State for Health and Social Care (England)	Welsh Government Minister	Scottish Government Minister	Northern Ireland Executive Minister
6 Delivers implementation	NHSE Screening Division & Regional Teams	Public Health Wales *(if designated lead)*	NHS Scotland and Public Health Scotland	PHA NI
7 Delivers evaluation	NHSE or DHSC	WSC *(performance review)* and PHW reports to WSC	Scotland NSC or Public Health Scotland	PHA NI reports to Northern Ireland SC
Number of laboratories	**13** (regional)	**1** (Cardiff)	**1** (Glasgow)	**1** (Belfast)
Most recent additions to panel implemented*	**January 2015**	**January 2015**	**March 2017**	**March 2020**

** A group of four rare conditions (MSUD, IVA, GA1 and HCU) were recommended by the UK NSC in May 2014, although when each nation began to screen for them varied.[19-21] From 2026, it is understood some of these stages may change.*

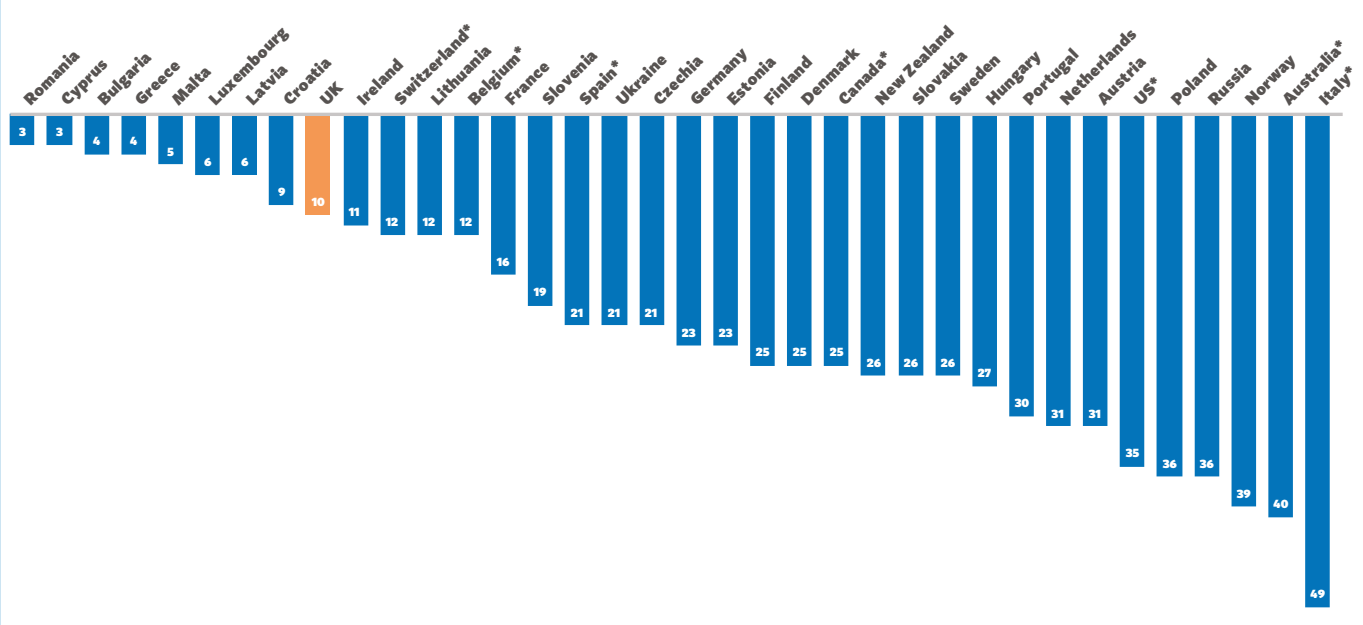
Why focus on decision-making for newborn screening in this report?

The UK is at a pivotal moment in deciding how to modernise its approach to newborn screening. In 2019, Genetic Alliance UK published a report to describe the views of its members on how to improve the timeliness of new additions to the UK's NHS Newborn Blood Spot Screening programme.[22] While the UK NSC review process is rigorous and evidence-based,[23] concerns were raised that this framework has limited utility when applied to screening newborns for rare conditions. Challenges were also identified around how representatives of people with rare conditions were consulted in decisions. In 2022, the set up of the UK NSC Blood Spot Task Group (BSTG) was a welcomed step in helping identify solutions to some of these challenges.[24] In the same year, tyrosinaemia type 1 (HT1) was recommended for inclusion, meaning the UK is now anticipated to screen for 10 conditions from 2026.[25] Recently, a new in-service evaluation (ISE) for multiple conditions (EQUIPOISE) was announced to be in the early stages of planning.[26, 27] The BSTG and genomic sequencing are also mentioned in England's 2025 Action Plan.[28]

Despite these developments, the UK screens for fewer conditions than similar programmes in other countries. Many European countries already screen for over 20 conditions. A survey of 32 countries reported that 90% had updated their screening panels between March 2021 and January 2024.[29] Examples include Italy, which nationally recommends screening for 49 conditions (with a further eight conditions anticipated),[30] and the Netherlands, which has implemented screening for 27 conditions.[31] Despite differences in health systems, Australia, New Zealand, the US, Canada and Japan also all routinely screen for over 20 conditions.[32] This is also the case in some countries navigating significant public health challenges, such as Ukraine and the Philippines, where the expansion of newborn screening programmes remains a priority.[33-35] The disparity between the UK's screening panel and these other countries has been described by a range of stakeholders.[36-45]

The number of conditions nationally recommended for newborn screening (May 2025)

While there are some nuances in definitions and exact numbers of conditions implemented (e.g. in-country variation, pilots, new additions) the below provides a sense of how the UK compares to other countries.



** National level recommendations only. Data from European countries surveyed in January 2024 by Charles River Associates[29] with updates from countries explored in this report (see table on page 11 for details).[46-66]*

Efforts to harmonise screening programmes across the UK continue to face challenges. Smaller populations and fewer resources relative to England constrain the ability of devolved nations to take part in pilots or ISEs while awaiting a UK NSC recommendation.[39] Timely action on recommendations is further impeded where infrastructural limitations may need to be addressed, as seen in the case of HT1.[25] Before this, the most recent recommendation by the UK NSC was in 2014 and it wasn't until 2020 that all four nations had completed implementation (*see table on page 11*). While in England several initiatives are evaluating whether to recommend screening for SCID and SMA, there have been delays,[67-69] leading to concerns that babies born with these conditions in other parts of the UK continue to go undetected.

The opportunity cost of deciding not to screen newborns for rare conditions is high. The global expansion of newborn screening panels signals that for many countries, screening for some rare conditions is not only clinically transformative, but economically sound. In the UK, there seems to be a concern that screening could increase NHS costs, but the cost of delayed diagnoses and late treatment are already in the system.[39] Even where modelling data for newborn screening is uncertain,[70-73] the logic holds. Over the 10 years before they received a diagnosis, people with rare conditions in England accounted for only ~1% of hospital patients but £3.4 billion in hospital costs (2017–2018).[74] This averages as £13,064 per person – more than double the cost for people who do not have a rare condition. Recent survey data for the UK indicates that 26% of people with rare conditions are unemployed,[10] nearly seven times the national average (4.1%).[75] As there are an estimated 3.5 million people in the UK living with rare conditions, screening could enable more timely treatment and improve health outcomes.

The widespread uptake of new technologies in healthcare present challenges to our decision-making function. The arrival of technologies for genetic newborn screening (gNBS), including genomic sequencing, and a growing need to address ethical, legal and social considerations in screening policy means that decisions are becoming more complex.[76-79] In England, the Generation Study is using whole genome sequencing (WGS) to screen 100,000 newborns to understand how we might improve our ability to detect and diagnose rare conditions.[80] Delivered by Genomics England in partnership with the NHS, the study represents a significant government investment in advancing and integrating genomic research into public health, an area of growing public interest.[81] It also signals a broader commitment to innovation, particularly for underserved or marginalised populations. Recruitment began in late 2024, and if there are findings from the study that offer the opportunity to learn how to improve outcomes for families affected by rare conditions, the UK needs to be prepared to respond.[82-84]

Supporting the UK's readiness to progress newborn screening

We acknowledge that comparing the number of conditions included in screening panels alone can be reductive as it may overlook the context within which decisions are made in different health systems.[85] Without prejudging the outcome of the research project, we know there are concerns from Genetic Alliance UK's membership that if findings from the Generation Study were to support changes to the current service, implementation may be slow or require further evidence. Public trust may also be undermined if we are not ready to meet the ambitions set out in the forthcoming NHS 10-Year Plan for England.* By gathering insights into how decision-makers in other countries approach these challenges, we aim to identify practical steps to support the UK's readiness to innovate and act on opportunities to detect rare conditions earlier. This way, the UK can ensure every child, regardless of where they're born, has the best possible start in life.

**This report was prepared in parallel to the NHS 10-Year Plan for England and written prior to its publication.*

Learning from decision-making processes in other countries

This report outlines findings from a research project exploring how decision-making for both genomic and conventional newborn screening is approached in different countries. A research framework was developed and applied to **14** countries (*below*) to gather insights from the peer-reviewed and grey literature and interviews with experts in newborn screening. A brief overview of the research questions applied to each country is in the Appendices *(page 30)*.

By taking a deeper look at how these countries balance rigour and pragmatism in their policy and processes for newborn screening, we have identified **five overarching areas** where there are opportunities for the UK's NHS Newborn Blood Spot Screening Programme.

Each theme groups practical learnings from how other countries have made both necessary and achievable adjustments to their decision-making processes to make progress in newborn screening for rare conditions.

Overview of countries where we applied the research framework (as of May 2025)

Country	Conditions recommended nationally*	Last update	Most recent additions	Genomic NBS pilots
Australia	40	2025	Biotinidase deficiency *(decision for 3 conditions pending)*	Yes
Canada	25 (core only)	2025	N/A *(9 additional conditions currently under review)*	No
Denmark	25	2024	CACT, CPT1, CPT2, HCU, Galactosemia, MPS I	No
Ireland	11	2023	SCID, SMA	No
Italy	49*	2025	SMA, SCID, Fabry, Gaucher, MPS I, X-ALD, Pompe *(to be confirmed)*	Yes
France	16	2025	SMA, SCID, VLCAD	Yes
Germany	23	2025	HCU, PA, MMA, vitamin B12 deficiency	Yes
Norway	39	2025	MLD, SCD and a group of 11 IMDs	No
Netherlands	31	2023	X-ALD	Yes
New Zealand	26	2025	SMA	Yes
Poland	36	2024	Pompe, Fabry, Gaucher, MPS I	Yes
Spain	21	2025	SMA, SCID, PA, MMA, VLCADD, IVA, HT1, OCTN2 deficiency	Yes
Sweden	26	2023	SMA	No
US	35 (core only)	2024	Krabbe *(US RUSP activity was paused in 2025)*	Yes

** Given variation within some countries, our research focused on the national level recommendations for screening and only 'core conditions' in the US RUSP and the new Pan-Canadian Newborn Screening List.[46-66] Italy currently recommends 49 conditions, but the eight conditions listed in the table are anticipated to be confirmed in the coming months.[30]* ***Please see page 31 for the full names of each condition in the above table.***

1 Evidence
Address constraints on reviewing rare conditions

Evidence requirements for rare conditions

Decisions must account for the fact that producing traditional evidence-based policy standards for screening, such as randomised-controlled trials (RCTs), is unachievable for most rare conditions in a reasonable time frame. While there is ongoing research into alternative approaches to evidence generation, such as modelling, these take time to scope, develop and refine. UK NSC guidance states that some types of evidence are only developed on a case-by-case basis.[87-89] However, some of Genetic Alliance UK's members have shared that allocating resources to fill evidence gaps did not result in a recommendation, and there are discrepancies in the threshold for evidence required by other UK healthcare decision-makers for the same question (e.g. clinical or cost-effectiveness of a treatment).[90-92] Some experts argue that waiting for a solution to measuring each condition's penetrance (extent to which a genetic variant will result in symptoms) and expressivity (the range or severity of symptoms) in a population, while helpful, will delay progress.[72, 43] To avoid decision paralysis, other countries accept the best available evidence on the basis that pursuit of a study that fully accounts for these variables is unworkable.

Use a pragmatic evidence threshold for reviews when natural history data is limited. Some countries have lowered the evidence bar just enough to make progress where the potential benefits are high, relying on expert opinion and early pilot outcomes to make conditional recommendations. Adopting a mindset of 'reasonable evidence is enough to start' will help ensure the UK moves forward with newborn screening.

In **Spain**, involvement of the national Health Technology Assessment (HTA) network to inform decisions and a decision matrix enabled rapid expansion of screening.[93]
- Norway applied the same cut-off values for evidence as Sweden to avoid requiring further pilots to expand its programme in 2012.[94]
- Ireland commissioned its HTA body to perform a review of international approaches to decision-making to develop a set of recommendations for newborn screening.[95]

Reduce duplication by leveraging real-world evidence from other countries. No single country can gather all the evidence alone and 'collect once, use often' has become best practice for rare conditions. Other countries engage in dialogue with one another, sharing data from pilots and condition reviews to strengthen their evidence base and avoid duplication. By trusting that the data used by partners is of equal validity, the UK can make more informed and timely decisions.

- Germany cited the importance of international pilots where local data is particularly limited (e.g. sickle cell) and jointly delivered a pilot for SCID with Poland.[96-98]
- New Zealand implemented screening for SCID in 2017 after deeming a local pilot was unnecessary, and cited evidence in Australia and the US informed its decision for SMA.[99-101]

Establish distinct review pathways for different categories of condition. Internationally, there is growing acceptance of a flexible, tiered evaluation process. Conditions with treatments currently delivered in the NHS should be distinguished from those with treatments on the horizon. Likewise, actionable conditions could be reviewed in a separate, lower priority pathway. Creating dedicated review tracks at the scoping stage could enable more timely decisions where immediate clinical benefit can be realised. Although definitions vary,[102] many countries (e.g. Australia, Canada, Germany, the Netherlands) have a list of 'target' (priority) conditions to implement within a set time-frame.

- Germany aims to implement four new 'target' conditions within 12 months.[59, 60]
- France prioritises conditions based on the strength of evidence available.[103]
- Australia made X-ALD for boys a target condition and referred X-ALD for girls for a more detailed technical review, recognising sex-specific differences in severity of the condition.[104]

Drive progress by closing evidence gaps between formal reviews, and **commit to a shorter review cycle where the need is urgent**. Some countries ensure that when a new therapy for a previously untreatable condition is approved, a decision can be made before the next scheduled review. Others have introduced laws or policies that encourage timely reconsideration, to accelerate access to new treatments. By looking at adaptive governance models in Europe where more flexibility is built in, the UK can craft a process where opportunities to act are not unnecessarily delayed, even if they fall between normally scheduled reviews.

- **Poland** and Norway expedited reviews of MLD and SMA in anticipation of new therapies.
- Germany's Federal Joint Committee (G-BA) holds open plenary sessions every few weeks; new evidence can also be raised in sub-committee meetings on an ad hoc basis.[29, 105]
- **Italy** established a legal framework to support more timely expansion of newborn screening.[106-108]

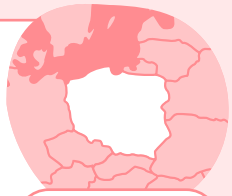
SPAIN

A more appropriate evidence threshold for newborn screening

The number of conditions nationally recommended in Spain is lower than what has been implemented by some autonomous regions (AR).[93] This variation widened from 2003–2020, a period in which HTA was introduced to support decision-making for newborn screening. To address this, the Ministry of Health commissioned a review that led to seven conditions being recommended for inclusion in its national programme in 2014. Building on this, Spain has recently been evaluating how to expand its offering to more than 20 conditions.[109] A framework for the expansion has been used to develop: (a) a uniform screening panel; (b) a decision matrix for expansion; (c) screening standards; (d) a common quality assurance process; and (e) a common information system linked to screening.[93] A further four conditions were included in 2022, and by the end of 2025 it is expected to reach 23 conditions.[64, 110]

	Number of conditions included in each regional newborn screening programme in Spain																
AR	Castilla-León	Asturias	Baleares	Canarias	Cantabria	Navarra	Valencia	País Vasco	Extremadura	Madrid	Castilla La Mancha	Cataluña	Aragón	La Rioja	Galicia	Andalucía	Murcia
2003*	3	3	3	2	2	2	3	2	5	3	4	3	3	3	25	3	3
2020	7	7	7	7	7	7	7	7	18	18	22	25	30	30	30	25	40

**The authors of the paper highlight caution should be applied to data from 2003 due to a lack of validated records.*[93]



POLAND

A pragmatic approach to evidence for rare conditions

Poland has rapidly expanded its national programme in recent years. It was an early adopter of biotinidase deficiency screening, noting the net benefits of intervention (a low-cost vitamin B7 supplement) outweighed the harms of potential overdiagnosis.[111] Poland has also been selective in conducting further pilots where data was lacking for a Central European population. From 2017 to 2020, it partnered with Germany to evaluate SCID screening in a pilot (Rare-Screen), using findings from its transborder area to locally validate international evidence.[96] A continuous approach to horizon scanning for international evidence and new therapies enabled the Ministry of Health to make a decision on SMA in March 2021, two years after a gene therapy was approved.[112] The following month, a pilot phase for SMA screening began and nationwide rollout was completed within 12 months.[113] A group of four lysosomal storage disorders was also approved in 2024, meaning the Polish national programme is expected to expand to 36 conditions by 2026.[114]

ITALY

A legal framework to mandate expansion of newborn screening

In 2016, Italy enacted Law No 167 to expand newborn screening and establish a coordination centre at the National Institute of Health (ISS), which included representatives from three patient organisations, including UNIAMO.[106-108] As a result, the number of nationally recommended conditions for screening increased from three (in 1992) to around 40. However, pilots and regional differences in infrastructural capacity have led to variation in how many conditions are screened for across the country.[115-117] In response to new therapies for rare conditions, an amendment to the original law was made in 2019 to expand its remit and allow for more frequent updates to the screening panel. Patient representatives were also invited to join a Ministry of Health working group to help identify and prioritise which new conditions to include. This enabled the current total of conditions recommended to reach 49, and the updated framework has helped ensure that nomination of new conditions: (1) promotes more timely expansion of regional programmes; (2) reflects both the needs and preferences of the rare disease community; and (3) respects the decision of local governments to implement when they are ready. A further eight additions are expected to be confirmed in 2025.[30, 63]

2 Partnership
Leverage the expertise of the rare community

The rare community's voice in decision-making

The UK NSC has made improvements to how it engages with the rare community by inviting selected representatives to the UK NSC's BSTG.[24] A recent increase in the frequency of blog posts related to newborn screening is also noted. However, since BSTG meetings are confidential, members are limited in what they can share with their community. While a 'partnership board' to scope out an ISE for SMA in England is promising,[68] some have expressed a lack of clarity around the board's activities and the delay starting.[118] More broadly, a lack of distinction between 'patient voice' and 'public voice' has also led to concerns that groups of stakeholders may be excluded. A recent stakeholder survey reports only 46% feel satisfied engaging with the UK NSC.[119]

It is also difficult to access guidance for new stakeholders. This means if consultations are overly long or technical, held at inconvenient times or not well-publicised, only a few with the necessary resources and networks may take part.[120] Consultations appear to be the main opportunity for stakeholders to engage with the UK NSC, although a date for when these are expected to open is not usually made public. In contrast, NICE offers numerous opportunities in both private and public forums (*below*).[121] Evidence accepted during NICE Highly Specialised Technology (HST) assessments, including 'expert witness' testimonies, also places clinicians, scientists and patient representatives on more equal footing.

PREPARATORY STAGE			DECISION-MAKING STAGE					POST-DECISION	
TOPIC SELECTION	SCOPING PHASE	EVIDENCE SUBMISSION	TECHNICAL ENGAGEMENT	COMMITTEE MEETING 1	CONSULT	COMMITTEE MEETING 2	FINAL DRAFT GUIDANCE	APPEAL	GUIDANCE PUBLISHED
Identify & select evaluation route	Identify appraisal focus areas	Collect evidence from affected stakeholders	Work through evidence and uncertainties	Make a draft decision IN PUBLIC	Invite input on draft decision	Discuss comments IN PUBLIC	The final decision IN PUBLIC	Final decision check	Guidance review
LAY MEMBERS on decision-making panel	PSOs consulted and invited to workshops	PSOs + PATIENT EXPERTS written submissions	PSOs comment PATIENT EXPERTS answer questions	PATIENT EXPERTS answer questions LAY MEMBERS in decision-making discussions	PSOs + PATIENT EXPERTS comment PUBLIC consultation	PATIENT EXPERTS invited back LAY MEMBERS in decision-making discussions	PSOs comment on factual inaccuracies and can appeal	PSOs can appeal	PSOs can share new evidence and are consulted on need for guidance updates

PSO: Patient support organisation. Figure adapted from Norburn et al. 2020[121] and NICE Patient Involvement Team.

Remove barriers to stakeholder participation. It is not enough to invite the input of a select few people living with rare conditions; governmental bodies must remove obstacles that prevent all stakeholders from contributing their expertise to decisions. Acknowledging there are barriers and taking steps towards a more participatory approach demonstrates that stakeholder consultation is not a token exercise but a genuine attempt to gather and value lived experience in shaping newborn screening policy.

- **Germany** has a patient coordination office that offers training, guidance and support with evidence applications.[122]
  - In Spain, four umbrella patient organisations were involved as collaborating experts in a review on the use of HTA to expand newborn screening.[93]
- **Canada** and New Zealand developed 'culturally safe' versions of their guidance to be more inclusive of communities that experience inequitable health outcomes.[62, 123]
  - Australia and New Zealand also clarify their processes in national policy frameworks.[124, 125]

Embed representation of people with rare conditions in all decision-making processes. Ensure the perspectives of the rare community around the societal value of screening beyond biomedical criteria, are fully captured when reviewing conditions. Many nations treat lived experience as a form of expertise in its own right, making stakeholders more likely to accept decisions as they know someone 'like them' was involved in making them. The UK should guarantee for newborn screening decisions that at least one committee member represents people affected by rare conditions.

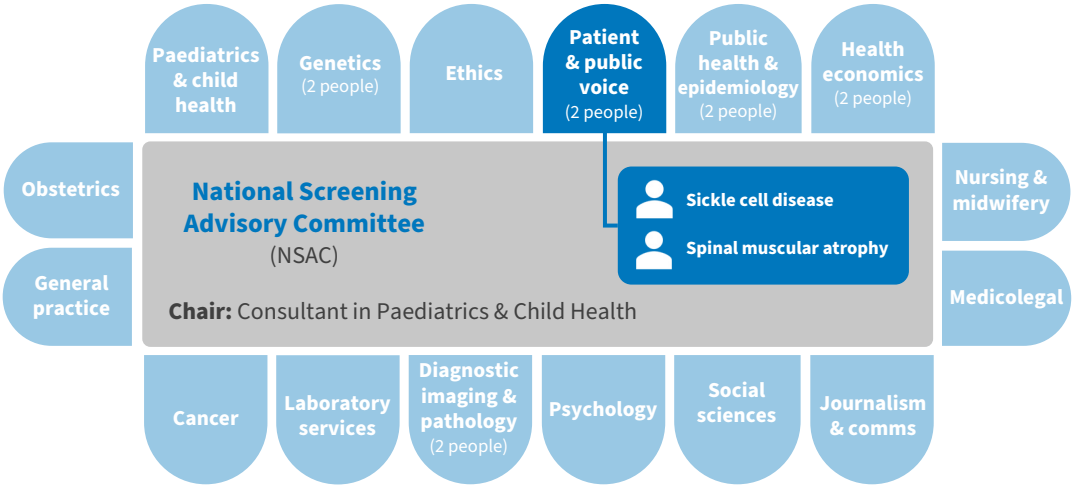
- A French umbrella patient organisation with over 200 members was given a seat on the national steering committee for newborn screening in 2024.[126]
- Italy formalised the role of three patient organisations in legislation to expand screening.[117]
- Sweden appointed a patient representative to its permanent expert panel responsible for producing the planning and prioritising of condition reviews.[127]

Partner with patient organisations to support timely implementation. Partnership also means crediting and trusting patient-derived knowledge, and there are opportunities to co-produce information to support parents with shared decision-making and consent. This is because patient organisations hold a wealth of clinical experience in conditions that are relatively unknown, and they are likely to be approached by families whose children are identified through screening. Opportunities for knowledge exchange between experts in rare conditions, some of whom may draw on their own experience of health services, may help streamline challenges around implementation that delay decisions.

- **Germany** has drawn on pilot data generated in partnership with patient organisations to inform its decisions to screen for several conditions.[128-130]
- French authorities partnered with a patient organisation to pilot SMA screening.[131]
- The SMA Newborn Screening Alliance developed a comprehensive toolkit to support implementation of SMA screening across several European countries.[113, 132]

A model of patient partnership for decision-making

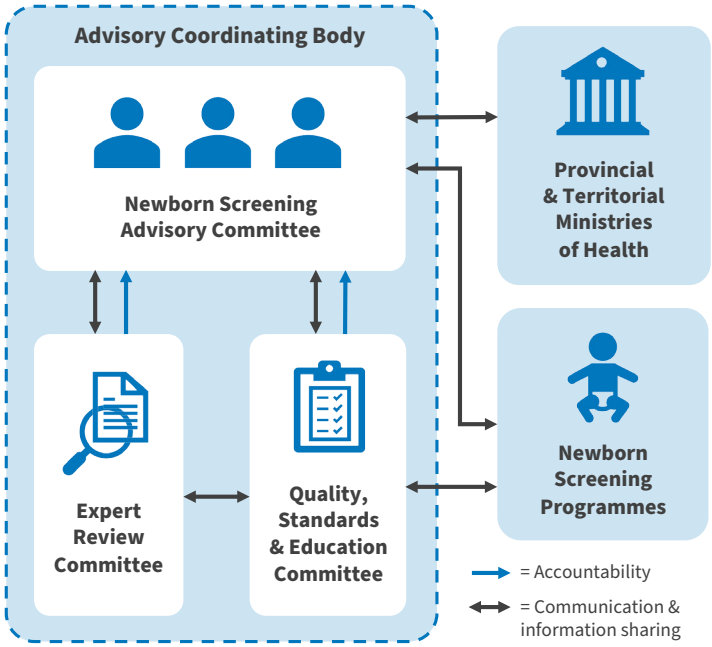
In 2019, Ireland established a National Screening Advisory Committee (NSAC). At the same time, the Minister for Health commissioned an international review of decision-making to inform a set of recommendations on the use of HTA for newborn screening, which were developed in consultation with patient advocates.[95] Two 'public voice' members that have expertise in rare conditions were later appointed to NSAC with equal voting rights.[133] However, expansion of the panel has been limited since NSAC was setup: one test was added to the panel and two more recommended for inclusion.[50] While concerns about the delay and inefficiencies around gathering evidence to inform decisions remain,[134] this shift towards more meaningful partnership with the rare community has been welcomed.



CANADA

An equity oriented governance model to promote uniformity

Building on reflections around equity in decision-making for newborn screening,[135] Canada's Drug Agency published draft guidance to cover all 10 provinces and three territories.[123] The guidance was developed in partnership with communities that have been made vulnerable by social or economic policies, including minority groups and people living with rare conditions. A new governance model was proposed to ensure these groups are represented in the three committees responsible for reviewing evidence and deciding which conditions are added to a 'Pan-Canadian Newborn Screening List'. Each committee will have two co-chairs and 11 members with diverse gender, racial and cultural backgrounds. The model underwent public consultation to ensure it also respects the autonomy of decision-makers in each jurisdiction to implement screening. An initial list has been proposed for 25 'core' conditions to align with the US, while nine others are under review.[86]



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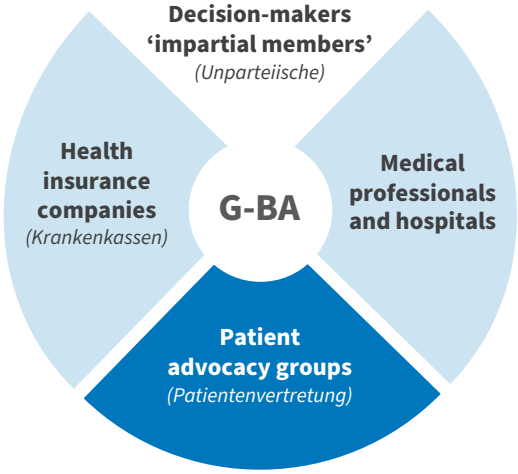
GERMANY

A patient involvement unit to address barriers to patient voice

In 2004, the German Federal Joint Committee (G-BA) setup a patient participation unit (Stabsstelle Patientenbeteiligung, SP) to embed patient voice into its decision-making processes, including for newborn screening.[136] Around 300 patient representatives formally engage in G-BA committees.[137] In agreement with the SP, four large patient umbrella organisations can appoint representatives and submit proposals for conditions to include in screening.[105] Patient representatives also support pilots and data collection (e.g. for SMA)[129] and often bring evidence from colleagues in other countries to meetings. Families affected by the condition being reviewed are also invited to present oral evidence in G-BA expert hearings. To facilitate this, a dedicated coordination office for the SP organises meetings, provides training, including methodological and legal advice, and offers support with discussion documents and nomination procedures.[122] This structure has supported patient-led proposals for new conditions to reach the screening agenda, such as HT1 (2014) and MLD (2024).[138, 139]



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3 Transparency
Ensure clarity in decision-making

Information on newborn screening decision-making

While the explicit outcomes from decisions published on the UK NSC's recommendations portal are clear, further steps can be taken. One of the challenges is ensuring a clear rationale is provided for negative recommendations when the evidence is noted to be supportive of screening. There are currently a large number of webpages that describe the governance for newborn screening decisions, but detail on the decision-making process is sometimes lacking. For example, several methodologies for how consensus is reached are described, but it is unclear which is used in practice. Public dissemination of new developments, including the status of ISEs or work carried out by UK NSC advisory groups, are often delayed and sometimes restricted to short (200 word) meeting summaries.[28] In early 2025, a number of conditions were listed as overdue for their next periodic review (*below*), but a new date for review or decision to reschedule is not public. As a result, many stakeholders that Genetic Alliance UK works with report finding it challenging to understand if progress on expanding newborn screening is being made in the UK, and which gaps in the evidence base they should direct their research and advocacy towards.[43]

Examples of conditions not recommended by the UK NSC (January 2025)[140]

Condition	Published	Summary rationale by UK NSC*	Next review due
ALD	2021	*'incidence of ALD in the UK'*	2024 – 2025
Amino acid metabolism disorders	2015	*'tests would identify some healthy babies as having the conditions when they do not'*	2021 – 2022
Biotinidase deficiency	2022	*'it is not known how many people in the UK have the condition; only limited evidence (not from the UK) was found on a range of different screening tests'*	2025 – 2026
CAH	2022	*'Further studies (ideally conducted in the UK) could help to improve the evidence relating to how good the tests are.'*	2025 – 2026
MLD	2023	*'The evidence map concluded that the available evidence on screening test accuracy and cost-effectiveness, though limited, is promising and warrants further review. It also found that the volume and type of evidence related to the benefits and/or harms of treatments in presymptomatic patients with MLD is sufficient to justify a more in-depth review of the evidence.'*	2026 – 2027

** Comments in this table were selected as they also demonstrate some of the challenges around evidence for rare conditions (page 12). Only select comments and conditions that received a non-recommendation have been included in this table for brevity. A recent analysis published by Rankin et al. (2025)[43] explores this in more depth.*

Adopt an objective scoring framework to strengthen trust in review outcomes. Decisions should be made systematically with each condition evaluated against clear, weighted criteria. A framework helps ensure consistency, highlight areas of uncertainty, and streamlines the process for stakeholders. Many countries have adopted decision matrices that grade evidence quality and anticipated benefit across clear domains, making the reasoning behind outcomes clearer. Frameworks also promote accountability, which potentially shortens the time to eventual approval if new evidence emerges to address the stated reasons for the initial non-recommendation.

- **The US** uses a decision matrix to evaluate and grade evidence for each condition.[66]
- Denmark uses a quantitative scoring matrix to understand to what extent a condition fell short of the threshold for recommendation (e.g. 60 out of 100 possible points).[141-143]
- France and Belgium also use a multi-criteria decision analysis model to select conditions for screening.[103, 144]

Publish materials to clarify how screening decisions were made. Publishing minutes and meeting materials demystifies the decision-making process; stakeholders can see whether a decision was unanimous or split, and which concerns were raised during the process that led to the final outcome. Some countries publish materials in a single, easy to navigate repository or document. It is especially important to clarify how methods were applied to evidence that result in a non-recommendation; once it is clear a decision wasn't an arbitrary 'no', efforts can be channelled into closing the evidence gap. This level of detail may seem granular, but it promotes trust that the process is systematic and open to future developments.

- In the US, a repository of all materials used to inform decisions are published.[145] In some states, this includes details of how individual committee members voted.
- The new pan-Canadian guidance outlines a decision-matrix and consensus voting approach will be published.[123] In the meantime, the Newborn Screening Ontario Advisory Council meets a minimum of four times per year and quorum is set at 50% + 1.[146]

Provide regular updates on the status of reviews and initiatives to manage expectations. A well-maintained and user-friendly public repository of resources is a simple but effective tool that can help signal that progress in expanding newborn screening is a priority. Frequently updating the repository with which conditions are under review, which are pending implementation and when the next review is due manages expectations. This way the community will be better informed at what stage a condition is, even if not approved yet, which may help address the perception that progress has stalled.

- The US and Australia have particularly detailed and user-friendly websites that share updates on the status of each condition.[46, 145, 147]

Improve accessibility by co-producing materials with patient organisations. Enabling frequent and accessible public consultations in newborn screening is in line with best practice by other decision-making bodies. In some countries, feedback from the process relayed that people felt their comments were addressing a known rationale and were valued.

- Canada consulted minority groups from different provinces to develop pan-Canadian guidance and a national list of conditions recommended for newborn screening.[123]
- **Australia** engaged the public in how to make their decision-making more transparent: 90% of responses to a public consultation supported the strategy to expand screening.[148]

NEW ZEALAND

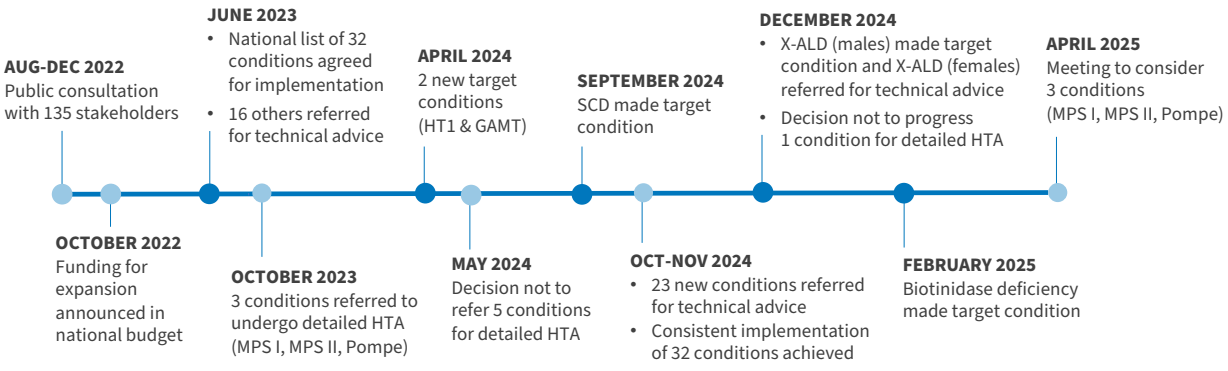
A lay-friendly National Policy Framework for newborn screening

New Zealand (Aotearoa) has screened for over 20 rare conditions in its national programme for almost two decades.[62] Biotinidase deficiency was first introduced in the 1980s and in 2006, a tandem mass spectrometer allowed the programme to rapidly expand to include an additional 21 conditions. In 2011, a policy framework for newborn screening was published to structure a clear process for evaluating conditions for inclusion.[125] If a nomination warrants further consideration, New Zealand collaborates with its international counterparts, particularly Australia and the US, to align on definitions and best practices to enhance the quality and consistency of its screening programme.[149] The framework also serves as a central document for new stakeholders to familiarise themselves with the processes involved and includes lay-friendly diagrams, nomination forms and named points of contact. In 2024, an update to the accompanying guidance to the framework was also published to improve the clarity and accessibility of language used for newborn screening decision-making.[62]

AUSTRALIA

Reform of a national decision-making pathway to accelerate progress

In 2018, the Australian government published a policy framework for newborn screening to end the 'postcode lottery',[124] and committed $107m AUD to expand its offering from 2022–2028.[104] A readiness assessment and public consultation informed development of plain-language guides and infographics on the proposed changes.[148, 153] To streamline the process, health ministers prioritised which conditions may need a more detailed review by its national screening committee by benchmarking its progress against international programmes with the highest number of conditions. From here, a list of 32 'target conditions' to implement were selected after agreement they had: (1) a specific and reliable test available; (2) well understood health outcomes; and (3) an effective treatment available. The website also shares regular updates on the status of each condition with timebound next steps.[46, 154] In just four years, all 85 conditions* in California's programme have either been considered or being considered for inclusion in Australia's national programme.[104] While this may require additional resources to replicate in the UK, it provides a compelling example of what could be achieved.



**Due to international differences in definitions, this is an equivalent of 76 conditions using Australia's classification system. This timeline has been redrawn with updates from the official sources.[46, 104]*

US

A structured approach to communicating more complex decisions

The US Health Resources and Services Administration's (HRSA's) advisory committee* for newborn screening makes decisions on the Recommended Uniform Screening Panel (RUSP).[66] Conditions reviewed for the RUSP are scored into four distinct categories with clear actions. The practice of publishing full transcripts and meeting materials promotes knowledge exchange and understanding of the rationale behind decisions.[145, 150]

Baby's First Test is an online resource that is part-funded by HRSA and run by a national patient organisation.[151] It visually summarises each state's progress and policies on newborn screening. This and similar resources (e.g. NORD's State Report Cards)[57] have been credited as helpful tools for stakeholders to monitor progress, engage with decision-makers and support more timely implementation in different US states.

ACHDNC
Advisory Committee on Heritable Disorders in Newborns and Children

Recommended Uniform Screening Panel Decision Matrix

	Magnitude of Net Benefit		
Certainty of Net Benefit	**Substantial**	**Moderate**	**Zero, Small or Negative**
High	**A**	**B**	**C**
Moderate	**B**	**B**	**C**
Low	**I (Insufficient)**		

Letter Grade	Description	Action
A	High certainty of substantial net benefit	Recommend addition to the RUSP
B	At least moderate certainty of at least moderate net benefit	Discuss and vote on recommending addition to the RUSP
C	At least moderate certainty of less than moderate net benefit	Do not recommend addition to the RUSP; Identify evidence gaps
I	Low certainty of net benefit	Do not recommended addition to the RUSP; Identify evidence gaps

Public Health Impact Assessment for implementation in 2 years	
% of states reporting effort required as high (# of states reporting high / # states reporting)	
% of states reporting effort required as moderate (# of states reporting moderate / # of states reporting)	
% of states reporting effort required as low (# of states reporting low / # of states reporting)	

**Genetic Alliance UK is aware of the recently announced policy changes in the US concerning the future of the Advisory Committee on Heritable Disorders in Newborns and Children (ACHDNC) that emerged during the drafting of this report.[152] These changes are not the focus of this report.*

4 Efficiency
Adopt an agile decision-making process

Readiness for innovation in screening technologies

The current approach in the UK relies on sequential review of individual conditions, which has led to some patient organisations feeling insufficiently resourced to prepare submissions and concerns that some of this work is being duplicated. Even when conditions meet UK NSC scientific criteria, additional evidence gathering to support implementation, such as qualitative research and cost-effectiveness models, appear to further delay decisions.[67-69] An example is SCID: first nominated for screening in 2011, an ISE started in 2021 and as of June 2025, a recommendation on whether to screen has not yet been made.[155] The planning of a multi-condition ISE under an approach called 'managed access to screening' is a promising development,[27] however limited information in the public domain about this process has led to some speculation around what it will involve.

More broadly, the UK's decision-making process remains relatively inflexible to conditional adoption of new technologies, presenting challenges for the UK to move towards improvements in both conventional newborn screening (e.g. new biochemical tests) and future screening techniques. As a result, some of the stakeholders that Genetic Alliance UK works with have shared concerns about the potential for widening inequities in health outcomes for people with rare conditions.

Take a proactive, opportunity-based approach to nominating conditions. Numerous countries have moved beyond a condition-by-condition review process, particularly when there are shared testing requirements across groups of conditions. Grouping and listing 'target' conditions not only improves transparency, but also helps move away from a reliance on stakeholders to trigger the review process. If the UK were to do the same, it could capture economies of scale in testing infrastructure and signal a clear commitment to expanding newborn screening.[46]

- Similar trends of recommending conditions by group are observed in Australia, Denmark, France, Germany, Italy, the Netherlands, Poland and Spain (*see table on page 11*).
- The Netherlands was the first European country to implement sex-specific screening for ALD in 2023,[156] adapting its approach to learnings from a pilot in New York.[157]

Decouple reviews of clinical evidence from decisions on implementation. Implementation is complex and can slow down decision-making. If the operational details need time to assess and scale, a staged approach would clarify where progress is stalled. This would also enable delivery partners to start preparations and carry out implementation research earlier to avoid delays for conditions with strong clinical justification. Further efficiencies can also be made when preparing to implement conditions with similar testing requirements.

- **The Netherlands** has split its decision-making pathway up into clear stages.[158]
- France has a two-tier process: HTA informs an opinion by its Health Authority (HAS), and a policy decision on implementation readiness lies with the national screening committee.[159]

Prepare for new technologies expected to transform screening programmes. As a public health strategy, screening programmes must be nimble and ready to meet the rapid pace of technological innovation that is ongoing in this space. The last major shift for newborn screening was two decades ago with tandem mass spectrometry (MS/MS), which helped many countries rapidly expand their testing infrastructure and the number of conditions they could screen for in one go.[160] Countries that were agile in their decision-making have reaped the rewards of new technology sooner, and genetic newborn screening (gNBS), including genomic sequencing, is the next such opportunity.[161] The value of gNBS is partly in its potential to screen for significantly higher numbers of conditions in parallel, a dimension of benefit that the UK's current condition-by-condition decision-making process cannot detect.

- The availability of MS/MS enabled Denmark, Norway, Italy, New Zealand and the Netherlands to rapidly expand their blood spot screening programmes before 2020.
- Australia's national policy framework for newborn screening considered the role of gNBS in 2018.[124] A readiness assessment was later commissioned and built on this.[153]

Globally, a number of countries are piloting gNBS to better understand some of the barriers to the technology being implemented into screening programmes.[162]

Ensure consistent, equitable access to newborn screening. Some larger or more devolved countries have established mechanisms to promote uniformity in which conditions are included in screening programmes at the national level. A number of international forums also bring together experts to share learnings on how to address and safeguard against widening disparities in access to screening between countries.[13, 163] Benchmarking can be a useful reference as to whether the UK is keeping step with opportunities in screening as a tool for early detection.

- Canada, Spain and Italy have introduced initiatives to promote more uniformity in the number of conditions implemented by their local governments *(see case studies)*.[86, 93, 107]
- Australia reformed its national decision-making pathway to end the 'newborn postcode lottery' by reviewing international programmes with the largest screening panels.[104, 164]

NETHERLANDS

A go/no go 'traffic light' framework for decisions

In 2015, the Dutch Health Council recommended a group of 14 new conditions for newborn screening (to total 31 conditions).[165, 166] Since the test for these conditions all used MS/MS, grouping them aimed to achieve economies of scale – training, equipment and protocols could be developed once rather than piecemeal, enabling laboratories to prepare to expand capacity in a more predictable way. A framework is used to advise when each condition would be ready to implement in the short-, medium- and long-term using a traffic-light checklist for questions on each condition.[158] Each condition passes through the same defined stages: evidence assessment by the Health Council, policy decision by the Ministry of Health, implementation planning by the National Institute for Public Health (RIVM), and evaluation by a separate body.[167] By splitting the decision-making process up, the system acts like a pipeline for steady expansion of newborn screening. Conditions most recently implemented in the Netherlands include: GALK (2020), SCID and MPS I (2021), SMA (2022) and X-ALD (2023). This means 27 conditions are implemented in the Dutch screening programme, with the fourteenth condition recommended in 2015 (OCTN2 deficiency) undergoing final review.[53]

A tool to streamline decision-making for similar conditions

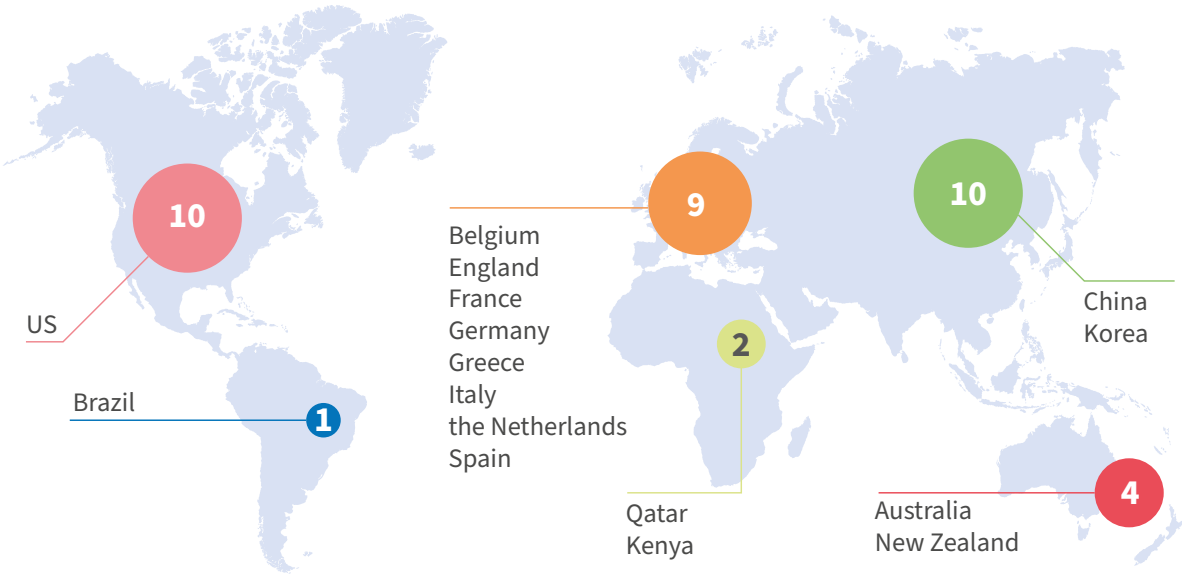
EUROPE

A group of UK and EU researchers have proposed the use of a novel decision-making tool to objectively assess and prioritise inherited metabolic disorders (IMDs) for inclusion in newborn screening programmes.[168] It employs a points-based system grounded in the original WHO criteria[169] for screening that is organised into three pillars: (1) details on the condition; (2) the screening test; and (3) progress in the availability of treatments. By scoring each, the algorithm aims to apply a structure to decision-making in anticipation of new developments on the horizon for rare conditions (e.g. new treatments or tests in the EU), and so promote more timely and efficient decisions. It also seeks to reduce disparities between countries and the burden on stakeholders to nominate or submit evidence to start reviews. The algorithm was tested on 48 IMDs, including 21 lysosomal storage disorders, that had been identified via review of expert consensus and whether they were included in screening panels in the US and eight countries with similar health expenditure per capita (Germany, Sweden, Austria, Australia, Iceland, New Zealand, Italy and Portugal).[170] Of these, 35 were concluded to be strong candidates for inclusion in European screening programmes.

GLOBAL

International readiness for genetic newborn screening

The International Consortium on Newborn Sequencing (ICoNS) aims to facilitate sharing of research into the real-world use of gNBS, including whole genome sequencing (WGS).[162] With over 500 members, including Genomics England, it seeks to promote greater consistency in how these technologies might be integrated into national screening programmes. Recently, members of ICoNS mapped more than 30 genomic newborn screening research or commercial programmes that are exploring how to expand the number of conditions that newborns are screened for (*below*).[58] A pilot of next-generation sequencing (NGS) is also underway in a number of European countries. Led by the Screen4Care initiative, it aims to screen 18,000 newborns for two panels of conditions, those that are treatable (TREAT) and those that are actionable (ACT), and explore the use of WGS as a complementary approach.[163]



5 Innovation
Embed newborn screening into health systems

Readiness for innovation in the life sciences landscape

The UK's pathway to deliver innovative medicines receives a great deal of attention, not least because of the tremendous unmet health needs of people living with rare conditions. The Innovative Licensing and Access Pathway (ILAP)[171] – now in its second phase of implementation – brings together key stakeholders to facilitate the passage of novel effective medicines through decision-making processes. To date, pre-symptomatic identification as the first stage in the clinical pathway of some medicines does not appear to have been a major factor in these initiatives, and it is not clear to what extent UK NSC is participating. While there is a 'horizon scanning function' of the UK NSC, it does not appear to be designed to facilitate wider uptake of innovation, as the experience of the SMA community demonstrates.[41] On the measure of conditions screened for using the blood spot test, the UK is so far behind nations with competing life-sciences sectors that it is potentially disadvantaged as a host for clinical research based on its capability to identify pre-symptomatic participants for clinical trials.

Establish an innovation pathway to ensure cross-sector collaboration. A more joined-up, system-wide approach to innovation in newborn screening policy can improve the UK's capacity to address barriers in the development of therapies for rare conditions. By ensuring alignment between screening policy and regulators like the MHRA and cost-effectiveness decision-makers (e.g. NICE, SMC), the UK can offer a clear, stable route for promising technologies for rare conditions to progress from research into clinical practice. For example, aligning with initiatives designed to promote UK innovation, such as MHRA's ILAP, might strengthen the UK's position to respond to emerging therapies in a more timely way.

- **Norway** was the first to start screening for MLD, having expedited its review in anticipation of a therapy (libmeldy) being approved by the European Medicines Agency.[4]
- Sweden has appointed a representative of people with rare conditions to its permanent expert panel which is responsible for horizon scanning for new developments.[127]

Support UK leadership to maximise opportunities that screening offers. Integrating data from newborn screening into wider research infrastructure (e.g. Genomics England, UK Biobank, NIHR and the Our Future Health study), would help deepen our understanding of the natural history of rare conditions. This, in turn, could support efforts to harmonise data collection across registries and enable the UK to address unmet needs by helping to de-risk early-stage therapy development and improve the evidence base for regulatory approval. It would signal to researchers and industry that the UK is a willing partner for innovation, particularly where small patient populations can mean investment is less attractive.

- **France** has launched a project involving gNBS screening that aims to also serve as an accelerator for developments in genomic medicine.[172]

An agile decision-making process to pioneer a new screening test

In 2012, legislation backed Norway's expansion of its newborn screening panel to 23 conditions, which was updated to 25 in 2018.[94] In early 2024, a public consultation on whether to add MLD was opened and by January 2025, Norway had begun screening for MLD – the first country in the world to do so.[4] To inform its decision, the committee drew upon evidence from: (1) pilot studies across Europe and the Middle East (where five babies were identified of 300,000 babies screened); (2) international consensus guidelines unanimously supporting MLD inclusion once early treatment was attainable;[4] and (3) the availability of a novel but validated three-tier screening test (involving two biochemical tests followed by targeted gene sequencing as the 'third layer'). While other countries also carried out regional pilots, Norway moved independently to prepare and align its recommendation with the European Medicines Agency's approval of a new therapy for early-onset MLD to ensure that lab diagnostic testing capacity and follow-up care pathways were prepared. Since January, Norway has further expanded its screening panel to 39 conditions, including a group of ultra-rare metabolic disorders.[52, 65] Norway's agile, evidence-driven approach offers a template for the UK to also leverage opportunities to innovate.

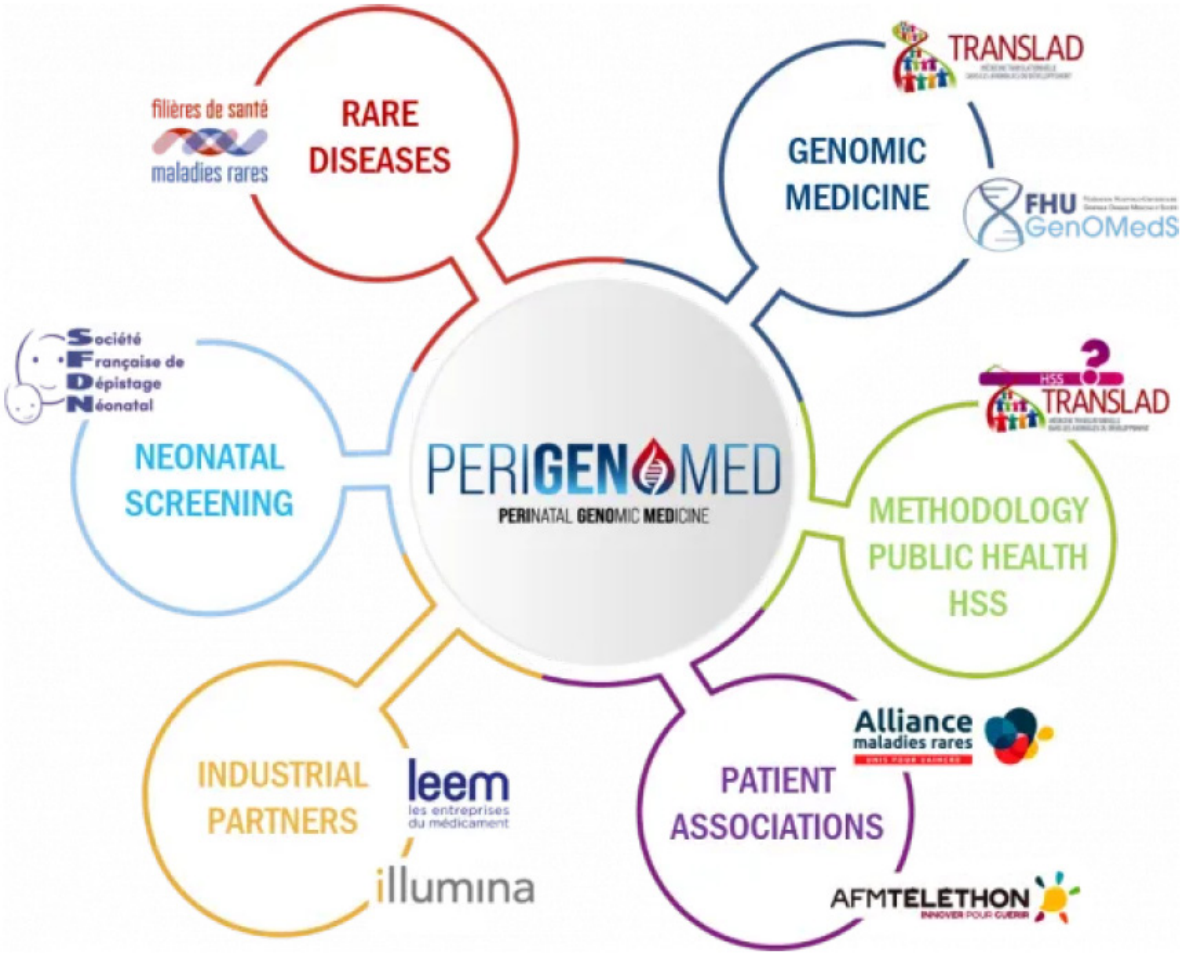
Building newborn screening into new tools for early diagnosis

Screen4Care is a five-year research programme being delivered by a large European public-private consortium, which includes partners in the UK and EURORDIS-Rare Diseases Europe.[163] The programme's 'dual approach' involves both a multi-country pilot for early detection via gNBS (*page 24*), and the development of digital tools that aim to support early diagnosis of rare conditions. For example, AI is being used to develop predictive algorithms to flag early signs of rare conditions within electronic health records, while a 'virtual clinic app' is being created to assist people with rare conditions after symptoms appear.[174] Qualitative and economic research into the impact of these technologies is also underway to inform development of a more sustainable model to address the 'diagnostic odyssey'.[7] The initiative demonstrates how newborn screening can be positioned as a key component to driving UK readiness for innovation to accelerate diagnosis pathways for rare conditions.

FRANCE

A partnership model to accelerate decisions and life sciences innovation

In France, the patient organisation AFM-Téléthon partnered with regional health authorities to deliver a pilot of targeted gNBS for SMA to enable more prompt treatment of children with the condition (before one month old).[131] Between 2022–2024, the pilot (DÉPISMA) screened over 85,000 newborns, of which eight babies were confirmed to have SMA. The partnership ensured that both laboratory and clinical challenges like false-positive cases were addressed in tandem. As a result, there were no false positive cases from screening and five babies received treatment with a gene therapy for SMA.[131] Its success, along with data from the US and Germany, informed the French Health Authority's (HAS) recommendation to expand France's panel in July 2024.[173] Building on this example, a project assessing the feasibility of genomic newborn screening (PERIGENOMED) has been designed in a participatory approach with patient organisations, national rare disease health networks, researchers and industry (*below*).[172] To meet the commitments in its National Plan for Rare Diseases, PERIGENOMED also aims to serve as an accelerator to support France to become a leader in genomic medicine.



Summary of learnings

1. Address constraints on reviewing rare conditions

If the UK adopts the same pragmatic ethos as other countries, there may be more willingness to greenlight reviews with moderate evidence where the potential benefit is compelling. By recognising that evidence generated in countries with reputable and rigorous review processes is of equal validity, the UK can make more informed and timely decisions. With a commitment to a time-bound mechanism for revisiting non-recommendations, the UK can craft a process where no opportunities to act are unnecessarily delayed.

2. Leverage the expertise of the rare community

Holding lived experience in parity of esteem would enhance the relevance of UK NSC decisions. When evidence challenges are addressed, the UK can benefit from a more impactful use of the rare community's expertise: co-development of real-world evidence and guidance to support implementation. The UK NSC BSTG and SMA Partnership Board are examples of positive change in this area. It is important to maintain this momentum and extend these approaches to people living with other rare conditions under review, including stakeholders who have not previously engaged in the process.

3. Ensure clarity in decision-making

Improving the accessibility of its processes would allow the UK to support more constructive engagement from patient organisations and clinicians in consultations. A 'how we made this decision' section of minutes would enhance transparency and enable stakeholders to make proposals to manage evidence gaps or address perceived risks.

4. Adopt an agile decision-making process

Advancing the proposed framework of 'managed access' to newborn screening could enable earlier, conditional use of new tests. This approach would allow people to benefit from new technologies sooner, while supporting the parallel generation of evidence for wider implementation. With an array of novel technologies on the horizon to support newborn screening, engaging in dialogue with experts in other countries would also streamline the review process for each condition.

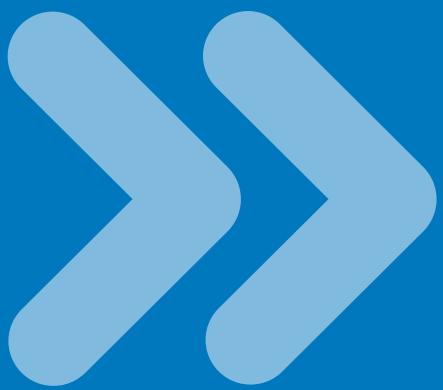
5. Embed newborn screening into health systems

Newborn screening should be recognised as an enabler of innovation across the rare disease landscape. Establishing a clear pathway for aligning screening with areas of innovation in genomics, regulatory processes and research would support early access to promising tests and therapies while collecting structured real-world data to support the evaluation of screening on health outcomes.

The UK must make a clear decision on its approach to newborn screening

Our review of other countries' approaches outlines a pathway for change, with case studies demonstrating how rapidly progress can be made. There is a real opportunity to grasp the potential of the Generation Study, deliver on the UK Rare Diseases Framework's screening commitments, advance the prevention theme of the NHS 10-Year Plan for England, and position screening as a key part of the Life Sciences ecosystem. With key strategies already pointing in this direction, it's time to act.

Appendices



Summary of the research methodology

Scoping research of peer-reviewed and grey literature on newborn screening decision-making was used to inform the development of the research methodology. With guidance from the six project advisors, research questions were organised into a framework (*below*) to structure how data was gathered for each country. Additional commentary from country experts was sought where possible within the timeframe for this project. Common themes from each country were grouped and drafted into a set of recommendations (learnings), which were shared with the project advisors, including members of the UK NSC, for input. A workshop with members of Rare Disease UK's Patient Empowerment Group (PEG) was held in April 2025 to refine these recommendations. All project advisors were invited to review the draft learnings and at least one draft of the report prior to finalisation.

1. What is the current status of newborn screening (NBS) in each country?

- How many conditions have been approved for NBS at the national level?
- Which conditions are approved?
- What year was each condition approved for NBS?
- Are there any ongoing pilots/studies – or have any been recommended?

2. How is evidence reviewed for decision-making around newborn screening?

2a. How is the national/regional screening committee (SC) governed?

- What legislation and guidelines exist to support newborn screening?
- How often do the SC convene and how transparent is this process?
- Have there been exceptions to the regular process – if so, what triggered these? (e.g. an unscheduled review)

2b. What is the process for reviewing evidence for decision-making?

- How are criteria for evidence submission described? (e.g. the publication of standards)
- Are there limitations around quality of evidence? (e.g. only RCTs)
- Once evidence is reviewed, what are the processes and criteria around this? (e.g. evidence is only considered once, there must be a set time period after review)
- Is evidence from other countries for decision making considered– if so, how?

3. What opportunities exist for patient voice in newborn screening decision-making?

3a. How is patient voice incorporated into decision-making for newborn screening?

- Is there a differentiation between public and patient voice (i.e. within the term 'PPV')?
- Do patients have a say in decision-making for newborn screening – if so, how?
- How are patients or patient representatives involved as decision makers?
- How are new stakeholders for patient voice onboarded to the process?
- What is known about the diversity of stakeholders involved in decision making? (e.g. size of organisations, representation of minority groups)
- What challenges have been raised around patient involvement?

3b. How is evidence from the patient community collected?

- Can patients submit evidence to the screening committee – if so, how?
- What methods are used to gather patient voice? (i.e. format)
- How frequent are opportunities to gather patient voice?
- Are invitations to join the consultation process proactive?
- How frequently is the list of stakeholders for patient voice reviewed?
- Can new stakeholders express an interest in joining the evidence process?

Report abbreviations and definitions

Full name of condition	
CACT	Carnitine/acylcarnitine translocase deficiency
CAH	Congenital adrenal hyperplasia
CHT	Congenital hypothyroidism
CPT1/2	Carnitine-palmitoyl transferase 1a or 2 deficiency
G6PDD	Glucose-6-Phosphate dehydrogenase deficiency
GA1	Glutaric aciduria type 1
GAMT	Guanidinoacetate methyltransferase
HCU	Homocystinuria
HT1	Hereditary tyrosinaemia type 1
IMD	Inherited metabolic diseases (group of conditions related to metabolism)
IVA	Isovaleric acidaemia
MCADD	Medium-chain acyl-CoA dehydrogenase deficiency
MLD	Metachromatic leukodystrophy
MPS I	Mucopolysaccharide disease type I (Hurler syndrome)
MPS II	Mucopolysaccharide disease type II (Hunter syndrome)
MSUD	Maple syrup urine disease
OCTN2	Primary carnitine deficiency, also known as Carnitine transporter deficiency (CUD)
PA	Propionic acidemia
SCD	Sickle cell disease
SCID	Severe combined immunodeficiency
SMA	Spinal muscular atrophy
X-ALD	X-linked adrenoleukodystrophy (ALD)

Other acronyms used in this report	
BSTG	Blood Spot Task Group of the UK NSC
DHSC	Department of Health and Social Care (UK)
G-BA	Gemeinsamer Bundesausschuss (German Federal Joint Committee)
gNBS	Genetic newborn screening (e.g. for specific genes using next-generation sequencing or whole genome sequencing)
HAS	Haute Autorité de Santé (French National Health Authority)
HTA	Health Technology Assessment
ISE	In-service evaluation (a UK NSC term)
ISS	Istituto Superiore di Sanitàto (Italian National Institute of Health)
MS/MS	Tandem mass spectrometry
NBS	Newborn screening
NICE	National Institute for Health and Care Excellence (UK)
NIHR	National Institute for Health Research (US)
NORD	National Organization for Rare Disorders (US)
NSAC	National Screening Advisory Committee (Ireland)
PPV	Patient and public voice (instead of patient and public involvement, PPIE)
PSO	Patient support organisation
RIVM	Rijksinstituut voor Volksgezondheid en Milieu (Dutch National Institute for Public Health and the Environment)
RUSP	Recommended Uniform Screening Panel (US)
SMC	Scottish Medicines Consortium
UK HSA	UK Health and Security Agency
UK NSC	UK National Screening Committee
UNIAMO	Federazione Italiana Malattie Rare Onlus (The Italian Federation of Rare Diseases)
WGS	Whole genome sequencing

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