UK National Screening Committee

UK National Screening Committee (UK NSC)

Newborn screening for biliary atresia (BA)

Date: 30 June 2026

Contents

Aim

This document provides background to the attached evidence summary on newborn screening (NBS) for biliary atresia.

UK NSC 2021 Evidence Map

Biliary atresia (BA) is a rare neonatal liver disease of unknown aetiology where inflamed and blocked bile ducts lead to a build-up of bile in the liver. Without treatment, the disease progresses rapidly and can cause death from liver disease within the first 2 years of life. There are approximately 37 cases of BA in the UK each year. The only treatment for BA is a surgical procedure termed Kasai portoenterostomy.

In 2020, the UK NSC recommendation on screening for BA was due for update. The most recent review prior to this was an evidence summary produced in 2017. In 2020, the UK NSC commissioned an evidence map to examine if there was sufficient new evidence to justify the commissioning of an evidence summary to address the evidence gaps highlighted by the 2017 UK NSC evidence summary; this evidence map was published in 2021. Prior to commissioning, a submission was received through the UK NSC open call for topics relating to screening for BA using stool colour cards (SCCs), a test not previously reviewed by the UK NSC. Therefore, additional questions on SCCs were included in the 2021 evidence map.

The evidence map addressed: 1) the evidence on using dried blood spots (DBS) to detect BA, 2) the accuracy of SCCs to detect BA, 3) whether screening for BA using SCCs improves time to surgery and clinical outcomes, and 4) the reported age at surgery/time to surgery for BA in the UK.

Overall, the evidence map concluded that there was sufficient evidence to justify commissioning an evidence summary.

UK NSC 2025 evidence summary

Aims

The aim of this 2025 evidence summary is to assess the volume, type, and direction of the evidence relevant to newborn screening for BA.

The 3 key questions addressed in this review are:

1. What is the accuracy of screening tests to detect BA in newborns?
2. What is the reported age at surgery/time to surgery for BA (Kasai portoenterostomy) in the UK?
3. Does screening for BA using stool colour cards improve time to surgery and clinical outcomes?

This evidence summary considers research published since January 2012 for questions 1 and 3, and research published since November 2016 for question 2.

Findings

For question 1, in relation to **UK NSC criterion 4**, *'There should be a simple, safe, precise and validated screening test'*:

For DBS testing, one systematic review and 3 individual studies were included in the evidence summary. Test performance results reported in these studies were limited. Sensitivities and specificities of over 90% were reported, but confidence intervals were wide, increasing uncertainty in the results.

For SCC testing, 2 systematic reviews and 5 individual studies were included in the evidence summary. These studies reported on the accuracy of SCC screening as part of screening programmes in several non-UK countries. There was a lack of consistency in the sensitivity results and positive predictive values (PPV) reported across different studies, reflecting the low numbers of BA cases and differing incidence between countries. The 2 studies reporting prevalence closest to the UK found PPV to be between 4% and 6%. The specificity and negative predictive value results were more consistent across studies and were generally high.

Limitations in the quantity, quality, consistency and applicability of the evidence available indicates that **criterion 4 is currently not met.**

For question 2, in relation to **UK NSC criterion 15**, '*Clinical management of the condition and patient outcomes should be optimised in all health care providers prior to participation in a screening programme'*:

The current evidence summary reported a median age at surgery in the UK of 51 days based on data up to 2019. The median age at surgery in the UK is comparable with the reported age at surgery in countries with stool colour card screening programmes. No data were identified to update the proportion of infants that have a late Kasai portoenterostomy in the UK.

Previous UK NSC evidence summaries found the median age at surgery to be 54 days, based on data up to 2009. **Criterion 15 was considered met in previous evidence summaries and is still met in the current evidence summary.**

For question 3, in relation to:

- **UK NSC criterion 11**, *'There should be evidence from high quality randomised controlled trials that the screening programme is effective in reducing mortality or morbidity'*:

  The studies identified consistently reported that time to surgery improved for infants with BA after the introduction of screening using SCCs. There also appeared to be a reduction in the proportion of infants receiving late surgery and improvement in other clinical outcomes, although the statistical and clinical significance of these outcomes was less clear. There was no indication within the included studies that screening using stool colour cards is likely to lead to harm. However, none of the studies identified used a randomised controlled trial design. **Therefore criterion 11 cannot be considered as met.**

- **UK NSC criterion 13**, '*The benefit gained by individuals from the screening programme should outweigh any harms, for example from overdiagnosis, overtreatment, false positives, false reassurance, uncertain findings and complications'*:

  In countries with screening, mean age at surgery after introducing SCC screening improved and ranged from 46 to 60 days. However, the applicability of the results of these studies to the UK context is uncertain as the age at surgery following the introduction of the screening programmes is similar to that reported in the UK without a screening programme being in place. **Therefore criterion 13 cannot be considered as met.**

A key question that is not answered by the current evidence is: what are the outcomes for babies diagnosed with BA in the UK under the current standard of care? We agree with stakeholders that median age at surgery does not tell the whole clinical story or inform us about the 'tail' of babies who receive a late intervention; however, we could not identify any more informative published sources of evidence. Without evidence on the outcomes for babies under the current system, including those who receive a timely or a late intervention and preferably stratified by age at surgery, it is not possible to determine the baseline upon which the potential benefits

and harms of screening can be overlaid. The UK NSC value new evidence in this area.

Clinical management of infant jaundice has improved in recent decades. If, as the available evidence suggests, the UK is diagnosing cases of BA relatively early, the potential benefits of screening are likely to be smaller and the balance of benefits and harms less favourable. Conversely, if this is not the case, the argument for screening is stronger. However, the current UK situation cannot be fully understood without further published evidence on outcomes in the UK; the UK NSC would welcome additional research in this area.

UK NSC recommendation

The volume, quality and direction of the new evidence published since the last UK NSC evidence summary suggests that the current recommendation not to introduce a UK systematic population screening programme for BA in newborns should be retained.

Action

The UK NSC is asked to note the consultation responses and approve the recommendation noted above that a population screening programme for BA should not be introduced.

Consultation

Background information

A 3-month consultation (25 February 2026 – 20 May 2026) was hosted on the UK NSC website. Direct emails were sent to 12 stakeholder organisations. **Annex A** contains a list of the 12 stakeholder organisations contacted.

The total number of separate consultation responses received was 4. Comments were received from the following stakeholders:

- Genetic Alliance UK
- British Association for the Study of the Liver (BASL)
- British Liver Trust
- Ipsen Ltd

The consultation comments received are presented below in **Annex B**.

Themes reflected in stakeholders' comments

Delayed diagnosis and clinical urgency of BA

A consistent theme across stakeholders' responses is concern about delayed diagnosis of BA and its impact on outcomes. Stakeholders emphasise that BA is a

time-critical condition where early detection is closely linked to improved prognosis, particularly in relation to timely Kasai portoenterostomy, and that missed or delayed diagnosis carries significant and irreversible consequences. They highlight that, in practice, delays still occur due to diagnostic uncertainty, misinterpretation of early symptoms such as prolonged jaundice, and variability in clinical recognition. This is reported to lead to later surgical intervention and, in some cases, liver transplantation. Stakeholders therefore argue that the current system does not reliably ensure early identification and that this represents a persistent unmet need.

Response

The UK NSC thanks stakeholders for highlighting concerns regarding delays in the diagnosis of BA and the importance of timely Kasai portoenterostomy.

The Committee recognises that BA is a time-critical condition and agrees that, in principle, earlier diagnosis is associated with improved outcomes. The evidence review also acknowledges that some delays in recognition can occur in routine clinical practice due to the non-specific nature of early symptoms and variability in presentation.

However, the current evidence indicates that, in the UK, the timing of Kasai portoenterostomy achieved without a population screening programme is already within the range associated with favourable outcomes. Recent UK data show that the median age at surgery is below 60 days, with further improvements observed in more recent cohorts. This is significant, as outcomes are generally considered optimal when surgery is performed within this timeframe.

Importantly, when compared internationally, the age at surgery in the UK is comparable to that reported in countries that have introduced population-based screening programmes (such as stool colour card initiatives). This suggests that the current system of clinical identification, supported by increased awareness and streamlined referral pathways, is performing at a level similar to that achieved through organised screening.

The UK NSC understands the concern raised by stakeholders that aggregate metrics such as median age at surgery may mask a subset of infants diagnosed too late to benefit optimally. The report acknowledges that a lack of data on the proportion of infants that have a late Kasai portoenterostomy is a limitation and calls for such data to be published. The currently available data suggests that while a small proportion of infants may still experience later diagnosis, and we thank stakeholders for sharing their experience of this, the overall trend in the UK has been towards earlier intervention over time, with relatively few cases undergoing surgery at a substantially delayed stage.

On this basis, although the concerns raised by stakeholders about diagnostic delay are understood, the available evidence does not indicate that the absence of population screening is resulting in systematically late intervention or poorer outcomes at a population level. The current timing of Kasai portoenterostomy in the

UK is therefore considered to be acceptable and consistent with good clinical outcomes.

Perceived gap between lived experience and UK NSC conclusions

Several stakeholders challenge the interpretation of the existing evidence base, arguing that the UK NSC conclusions do not fully reflect lived experience. There is a perception that current conclusions underestimate the lived experience of families and the variability in outcomes, particularly the “tail” of late presenters. Patient groups and charities report ongoing cases of late diagnosis and variability in care. As such, stakeholders question whether the current evidence assessment fully captures clinically meaningful gaps in the pathway.

Response

We understand that when newborn screening could have mitigated the devastating effect of BA, it can be difficult for families to accept that testing for the condition is not being prioritised for implementation. However, the UK NSC has to think about the implications of screening when it will be offered to hundreds of thousands of babies. For this reason, introducing a national population screening programme must be based on systematically reviewed evidence to ensure that screening brings more benefit than harm at a population level.

The lived experiences of children and families play an extremely important role in the committee's assessment of the evidence on the balance of potential benefits and harms of a screening programme. However, this particular review was focused on specific technical questions that need answering before further work on BA screening can proceed. Once the population-level effectiveness of a potential screening programme is established, lived experience becomes particularly important in shaping how a programme would be delivered.

The UK NSC will continue to keep the evidence for BA under review as part of its regular review cycle. We really value previous stakeholder comments when we scope our reviews, and the comments received during this public consultation will inform our next review. In addition, the Committee is actively exploring new approaches across a broad range of newborn blood spot conditions to help researchers expand the evidence base.

Screening test validity and emerging evidence (SCC and bilirubin-based approaches)

Stakeholders raise concerns that the review may undervalue emerging evidence on screening test performance. In particular, they argue that SCC and bilirubin-based approaches show promise, with evidence suggesting biological plausibility and, in some cases, high sensitivity. Some stakeholders distinguish between uncertainty around *implementation* and uncertainty around *test validity*, suggesting that the latter may be more established than reflected in the review.

Stakeholders generally consider the potential harms of screening to be low, particularly for relatively simple interventions such as SCC. They note that FP rates appear limited and argue that early identification of other liver conditions may represent a clinical benefit rather than harm.

There are also calls to consider a broader range of screening approaches, including conjugated bilirubin testing, which stakeholders argue may have been under-represented or excluded from the review scope.

Response

Thank you for your comments highlighting the emerging evidence on screening test performance for BA, including SCC and bilirubin-based approaches. The review examined both SCC and bilirubin-based DBS tests and acknowledged that both show biological plausibility with some studies reporting high sensitivity.

Although screening approaches such as SCC are relatively simple, the interpretation of SCC as a population screening tool is limited by important uncertainties in the evidence base. There was a lack of consistency in the sensitivity estimates for SCC reported across studies, with results varying widely between settings. Where confidence intervals were reported, these were often wide, reflecting the small number of BA cases identified and the resulting uncertainty in the estimates.

There was also notable variation in the PPV, which reflects differences in the underlying incidence of BA across countries. Two studies reported PPVs for prevalence levels more applicable to the UK, and these were relatively low, in the range of approximately 4% to 6%. This indicates that a substantial proportion of infants with a positive screening result would not have BA and would require further assessment. These false positives can lead to potential harms, including unnecessary blood tests, imaging, referral to specialist services, and parental anxiety while BA is being ruled out.

By contrast, specificity and NPV were more consistent across studies and were generally high. While this suggests that SCC performs well in ruling out disease, these metrics are less informative in the context of screening if sensitivity is uncertain and PPV is low in the target population.

In addition, while earlier diagnosis is reported in some settings, there is limited evidence of a clear improvement in longer-term clinical outcomes, and current UK outcomes are already comparable to those seen in screened populations.

Taken together, the review did not conclude that SCC lack promise, but rather that the current evidence base shows variability and uncertainty in key performance measures, particularly sensitivity and PPV, and limited direct applicability to the UK context. This underpins the cautious interpretation presented in the review.

The review acknowledges that evidence on bilirubin-based approaches is evolving and should continue to be monitored, alongside consideration of a broader range of

potential screening strategies as the evidence base develops. Although the review focussed on bilirubin-based approaches using DBS, studies examining bilirubin measurements in serum blood were also discussed. DBS-based screening is the preferred method of biochemical screening in newborns in the UK and worldwide. In contrast, serum-based newborn screening would require a venous blood draw, which raises numerous practical and acceptability issues.

Reliance on high-level evidence (RCTs) and appropriateness for rare diseases

A prominent issue raised is the perceived reliance on randomised controlled trials (RCTs) as a threshold for demonstrating programme effectiveness. Stakeholders argue that such evidentiary requirements may be disproportionate and impractical for rare, rapidly progressive neonatal conditions like BA, where randomisation may be ethically or logistically challenging. They suggest that observational, population-level, and international programme data should be given greater weight, in line with practices adopted in other screening contexts. This concern extends to a broader perception that current methodological expectations may delay decision-making in rare diseases.

Response

The points made about the difficulty of generating a high-quality evidence base in rare diseases are well made. The UK NSC recognises that generating RCT evidence for rare conditions such as BA can be challenging. However, because screening programmes are applied to very large populations, including many healthy individuals, the Committee applies a high evidence bar to ensure that benefits outweigh potential harms.

This does not mean that RCT evidence is always required; the criterion relating to the need for RCT evidence is not rigorously applied in evaluations of rare diseases. As for other rare conditions, the UK NSC review process was followed in this review. UK NSC evidence summaries are developed using rapid review methodologies. They provide an evaluation of the volume and direction of the literature on a single question or set of questions on a given screening topic. The evidence review process has been developed following the recommendation by the parliamentary Science and Technology Committee in 2014 and is published on a GOV.UK webpage available to the public: https://www.gov.uk/government/publications/uk-nsc-evidence-review-process/uk-nsc-evidence-review-process

The UK NSC considers the full range of available evidence, including observational, population-level, and international programme data, particularly where RCTs are not feasible. In this review, this included, for example, large population-based screening programme data and cohort studies from countries such as Taiwan, Japan and Canada evaluating stool colour card implementation and its impact on timing of diagnosis and outcomes.

However, the available observational evidence has limitations, including variability in study quality, potential bias, and differences in healthcare systems and disease

incidence that affect applicability to the UK. In addition, evidence of improvement in longer-term clinical outcomes remains limited.

Overall, the use of a high evidence standard reflects the scale and potential impact of screening, rather than a strict reliance on RCTs. The UK NSC has a 3-year review cycle to ensure we can regularly review the hundreds of conditions the committee has made recommendations on. However, if significant new evidence shifts the balance of benefits and harms in favour of screening, then a recommendation can be revisited before 3 years if necessary. If significant evidence is published in between regular reviews, individuals or organisations can submit proposals for an early topic update via the UK NSC's open call for topics process. If stakeholders become aware of published evidence to address the evidence gaps identified in the evidence review on BA, we encourage you to submit it via the open call for topics.

International evidence and implementation experience

Many stakeholders highlight international experience as an important and underutilised source of evidence. They note that screening programmes using SCC or other approaches have been implemented in multiple countries, including in Europe, and have been associated with earlier diagnosis and improvements in surgical timing in some settings. Stakeholders argue that international adoption, policy decisions, and real-world implementation should be more systematically considered within UK NSC assessments, particularly where UK-specific evidence is limited. There is also concern that current reviews may incompletely represent the extent of international practice.

Response

The UK National Screening Committee (UK NSC) does not exclude international evidence. In this review, studies from countries with established screening programmes (including Taiwan, Japan and Canada) were identified, included and systematically assessed, including evidence on diagnostic performance, age at surgery and clinical outcomes. However, a key part of the UK NSC assessment is determining how applicable this evidence is to the UK context. The NHS differs from other healthcare systems in terms of population characteristics, underlying incidence of BA, care pathways, and service delivery. As a result, findings from international programmes may not be directly transferable to the UK.

For example, some countries reporting improvements in surgical timing following introduction of stool colour card programmes operate in settings with a higher incidence of BA or different neonatal care pathways. In addition, the age at surgery reported on some of these programmes is broadly comparable to that already achieved in the UK without a national screening programme, which limits the extent to which these findings can be generalised.

We thank one stakeholder for raising that Germany has included SCC in their 'Yellow Booklet' nationwide and agree that the programme in Germany should not be referred to as a pilot. We have amended this in the report. In relation to the

screening programme in Germany, a peer reviewed publication (Madadi-Sanjani et al. 2021) was identified and included in the 2025 UK NSC evidence summary. This paper describes the piloting of a voluntary SCC screening programme in Lower-Saxony, Germany, and reports that of 13 infants diagnosed with BA during a 3-year period, 7 had received a SCC and one infant was identified on the basis of the SCC result.

No publications that met the criteria for inclusion in the 2025 evidence summary were identified for screening programmes in Switzerland or France.

Therefore, international evidence is actively sought and considered within UK NSC reviews. However, its relevance and transferability to the UK population and NHS system are carefully appraised to ensure that any recommendations are appropriate for the UK context.

Scope and inclusivity of the evidence review

Stakeholders raise methodological concerns about the scope of the evidence review. These include the exclusion of non-English language studies, grey literature, and certain types of implementation evidence, which stakeholders suggest may disproportionately affect rare conditions where evidence is often limited or not published in traditional formats. There are also questions about the exclusion of alternative screening strategies and whether the review scope reflects emerging developments in the field. Collectively, these concerns reflect a view that the current approach may omit relevant evidence and contribute to recurring evidence gaps.

Response

The scope of the review was defined in line with the UK NSC evidence review process and was informed directly by a stakeholder submission. Specifically, a request was received through the UK NSC open call for topics to consider SCCs as a potential screening test for BA, alongside an update of the previous evidence summary (2017).

In response to this request, an evidence map was commissioned to determine whether sufficient new evidence was available to support a full review. This evidence map explicitly addressed:

- the use of dried blood spots (DBS) to detect BA
- the accuracy of SCCs
- whether screening using SCCs improves time to surgery and clinical outcomes
- the reported age at surgery/time to surgery in the UK

The subsequent evidence summary was then designed around these questions, focusing on areas where stakeholders had identified potential developments and evidence gaps.

As noted earlier in this document, screening programmes are applied to very large populations, most of whom will never develop the condition. Because of this scale, even small harms can affect many individuals. The Committee applies a high evidence bar to ensure that benefits of screening outweigh potential harms, which includes requiring recommendations to be underpinned by high-quality peer-reviewed research.

In line with the UK NSC evidence review process, predefined inclusion and exclusion criteria were applied to ensure that the review was systematic, transparent and focused on evidence most relevant to assessing screening against UK NSC criteria. While stakeholders raise important points about non-English language studies, grey literature and implementation evidence, the use of structured methods and criteria is intended to ensure consistency and minimise bias across reviews.

Programme feasibility and NHS readiness

Several responses argue that screening for BA could be feasibly implemented within existing NHS infrastructure. Stakeholders point to the established DBS programme, existing clinical pathways for managing neonatal jaundice, and centralised specialist services as enabling factors. They suggest that logistical concerns could be addressed through integration with routine contacts (e.g. health visitor checks) and that screening could provide a more objective and standardised approach to detection. This is framed as an opportunity to improve equity, particularly where clinical recognition may vary.

Response

The UK NSC recognises that elements of the current system, such as the established DBS programme, existing pathways for managing neonatal jaundice, and centralised specialist services, provide a strong foundation for early identification and management. However, the evidence review found that outcomes achieved through these existing pathways are already comparable to those reported in countries with screening programmes. In particular, the age at surgery in the UK is similar to that observed following the introduction of screening in other settings

While a screening programme could offer a more standardised or objective approach to detection, the available evidence does not yet demonstrate that this would lead to meaningful improvements in clinical outcomes beyond current practice. In addition, evidence on the accuracy and real-world performance of potential screening tests (including DBS-based approaches) remains limited and uncertain.

As highlighted in discussions, including those within the UK NSC blood spot group, feasibility of integration alone is not sufficient to support implementation. The UK NSC has 20 criteria for a population screening programme. While several of the criteria relate to implementation, UK NSC evidence reviews typically focus on a limited set of questions related to the test and intervention (in screened groups), and screening programme. This is logical because a screening programme should not be

implemented without robust evidence that it is likely to be clinically and cost effective. Any new screening programme must demonstrate clear additional benefit at the population level and an acceptable balance of benefits and harms. Should a large-scale evaluation or roll-out of screening for BA be recommended in the future, then factors relating to implementation would be carefully considered.

Need for a more proactive approach to evidence generation (pilots, conditional recommendations)

A strong and recurring recommendation is for a more proactive approach to evidence generation and decision-making. Stakeholders advocate for pilot studies, phased implementation, or in-service evaluations to generate UK-specific data, rather than maintaining a no-screening recommendation in the absence of evidence. They argue that this would allow the UK to contribute to the evidence base while addressing uncertainty in a controlled manner. This is often framed within a broader call for a more flexible and proportionate approach to screening decisions in rare conditions.

Response

Making screening recommendations about rare diseases is difficult because of significant limitations in the evidence base. The UK NSC recognises the importance of developing UK-specific evidence for rare conditions such as BA, and the potential value of approaches such as pilots or in-service evaluations. However, decisions on screening are guided by the need to ensure sufficient evidence of benefit, and an acceptable balance of benefits and harms, before implementation.

The current evidence review highlights ongoing uncertainty around test performance, effectiveness, and overall impact on outcomes, meaning there is not yet a clear indication that screening would provide additional benefit over existing UK pathways.

The UK NSC evidence review process is designed to support proportionate and staged decision-making. For example:

- stakeholder submissions inform the scope of reviews. For example, calls to consider SCCs informed the review questions for the current evidence summary
- evidence mapping is used to determine whether sufficient data exist to justify a full review
- structured evidence summaries then assess screening against predefined criteria (e.g. test accuracy, effectiveness, and balance of benefits and harms)

Where pilot or phased implementation is suggested, these would still need to be undertaken within appropriate research and governance frameworks to ensure robust and generalisable findings. Therefore, implementation without sufficient

underlying evidence risks introducing a programme where benefits are uncertain and harms are not fully understood.

The UK NSC supports further evidence generation, including well-designed studies in UK settings where appropriate. However, introduction of screening, even in a pilot form, requires sufficient prior evidence to ensure that any programme is justified, safe, and capable of delivering meaningful population benefit.

Furthermore, BA will remain on the list of conditions which the UK NSC regularly reviews.

Awareness, education, and system factors

Stakeholders highlight the role of awareness and education in improving early detection. They report variability in healthcare professional recognition of BA and limited parental awareness of key signs such as stool colour and prolonged jaundice. Tools such as stool colour charts and information materials are seen as potential mechanisms to support earlier identification, both as part of screening and as adjuncts to routine care. This reflects a wider view that system-level factors, including training and communication, contribute to diagnostic delays.

Response

The UK NSC recognises the importance of these issues. Consultation responses across screening topics consistently highlight variability in healthcare professional recognition, low public awareness of key symptoms, and inconsistencies in clinical pathways as contributors to delayed diagnosis.

The Committee acknowledges that improving awareness of key signs (such as prolonged jaundice or abnormal stool colour), strengthening professional training, and providing clear information for parents could support earlier identification. Tools such as stool colour charts or targeted information materials may therefore have a role as adjuncts to routine care.

These considerations relate primarily to optimisation of existing clinical pathways rather than demonstrating the effectiveness of a population screening programme. Changes to clinical pathways are outside of the remit of the UK NSC and we kindly direct stakeholders to discuss their concerns with the National Institute for Health and Care Excellence (NICE). However, the UK NSC notes the strong public support for routine screening and the arguments presented regarding potential benefits, including earlier diagnosis, reduced uncertainty, and improved preparedness for families. The Committee also recognises calls for improved education, preventive guidance, and clearer clinical pathways, and notes that these issues highlight broader concerns around awareness, consistency of care, and post-diagnostic support within current services. The UK NSC also notes the need for national standardisation of follow-up and management practices.

Annex A: List of organisations contacted

1. British Association for Study of the Liver
2. British Association of Perinatal Medicine
3. British Liver Nurses' Forum
4. Children's Liver Disease Foundation
5. Genetic Alliance UK
6. Royal College of General Practitioners
7. Royal College of Midwives
8. Royal College of Paediatrics and Child Health
9. Royal College of Physicians
10. Royal College of Physicians and Surgeons of Glasgow
11. Royal College of Physicians of Edinburgh
12. The British Liver Trust

Annex B: Consultation comments

#	Submitter name	Organisation (if applicable)	Consultation response
S1	Dani Bancroft	Genetic Alliance UK	Genetic Alliance UK thanks the UK NSC for the opportunity to comment on this review. While we most often respond to consultations relating to rare conditions considered for newborn blood spot screening, we recognise that biliary atresia is also a rare condition where early identification is critical to outcomes. Our member organisations, including the British Liver Trust and the Children's Liver Disease Foundation, support families affected by this condition and see first-hand the devastating harm caused by delayed diagnosis and missed opportunities for early intervention. In short, biliary atresia is a rare, serious and time-critical condition where early detection is known to influence outcomes. Stool colour card screening represents a low-cost, low-risk intervention already implemented across multiple health systems. Consistent with the recommendations in our July 2025 report 'Time to decide: learning from international approaches to newborn screening decision-making', we encourage the UK NSC to adopt a more proportionate and adaptive approach to its evidence review process, including upfront consideration of a UK pilot or in-service evaluation. As we note on p.6 and p.12 of our report, rare conditions require a more flexible approach to evidence thresholds and a stronger emphasis on real-world and international evidence, as well as a more timely and efficient review process to address delays to expansion of screening programmes for rare conditions: geneticalliance.org.uk/wp-content/uploads/2025/07/Time-to-decide-Learning-from-international-approaches-newborn-screening-decision-making_Highres-3.pdf Our specific comments are outlined below. [p.8] 'National screening programmes using stool colour cards have been implemented in Taiwan and Japan…' We suggest that the framing of international implementation is incomplete. Stool colour card screening has also been implemented beyond these settings, including national or near-national approaches in Europe. For example, the Swiss Paediatric Liver Centre has published details of its national screening approach embedded within routine infant care here: www.hug.ch/en/csfe/screening/screening-and-biliary-atresia-screening-program. This broader implementation context is directly relevant to criterion 11. As we note on p.9 of Time to decide, international adoption decisions themselves are a critical form of evidence in rare conditions and should be more systematically incorporated into UK NSC decision-making.

			[p.8–9] 'Regional or pilot screening programmes… including… Germany.' We suggest that describing Germany as a pilot setting may understate current practice. Stool colour charts have been integrated into Germany's national child health booklet (Yellow Booklet), making them available to all newborns. Hannover Medical School reported on this implementation here: www.mhh.de/en/presse/mhh-insight/news-detailed-view/early-detection-in-babies-stool-colour-chart-becomes-part-of-the-yellow-book (published 2023). In addition, Germany's Federal Joint Committee (G-BA) has published supporting policy documentation on this screening approach here: www.g-ba.de/downloads/40-268-9634/2023-05-12_Kinder-RL_Ueberpruefung-Frueherkennung-Gallengangatresie_ZD-Anlage.pdf (2023). This reflects progression from pilot to routine implementation. As we highlight on p.9 of Time to decide, UK decision-making should remain responsive to evolving international practice rather than relying on classifications that may no longer reflect current reality. [p.10] 'No data were identified to update the proportion of infants that have a late (>60 days and >90 days) Kasai portoenterostomy in the UK.' We consider this a significant gap. Median age at surgery alone may obscure infants diagnosed too late to benefit from optimal outcomes. International evidence shows screening programmes were introduced specifically to reduce delayed Kasai procedures. For example, Taiwan's population-based screening programme demonstrated earlier referral and improved surgical timing: www.biliscreen.org/frontend_assets/Hsiao_et_al._Hepatology_2008.pdf As we note on p.12 of Time to decide, absence of UK data should prompt targeted data collection, pilots or in-service evaluation rather than supporting a precautionary non-recommendation. [p.10] 'none of the studies identified used a randomised controlled trial design. Therefore criterion 11 cannot be considered as met.' We suggest that reliance on RCT evidence is disproportionate in the context of a rare, time-critical condition. The reasoning for this is that population-based evidence from Taiwan and Japan consistently demonstrates earlier diagnosis and improved outcomes without RCTs, for example: www.jpeds.com/article/S0022-3476(14)01232-3/pdf. As we set out on p.6 and p.15 of our report, and as acknowledged by the UK NSC, requiring RCT-level evidence for rare conditions is often unrealistic and can delay access to interventions where benefits are already well understood and harms are low. This remark from the reviewers does not appear to recognise that the UK NSC's thinking has moved on to reflect this and leads us to be concerned that the research scope and proposed methodology for the third-party supplier of the evidence review may have been initiated and designed with this dated lens and potential bias from the outset. We strongly encourage the UK

			NSC to address concerns about this in its next committee meeting and to carry out an urgent review of its process for working with third-party evidence reviewers, to ensure that future (and ongoing) evidence reviews are course-corrected to reflect current thinking by the UK NSC. [p.9] 'there was no indication that the screening programmes are likely to lead to harm.' We welcome this finding. However, we suggest that the low likelihood of harm is not sufficiently reflected in the overall conclusion. Where screening is low-cost and low-risk, and benefits are time-critical, greater weight should be given to feasibility and early outcome improvements observed internationally. This aligns with our recommendation on p.6 of Time to decide that screening decisions should be based on proportionate risk-benefit assessments rather than absolute evidential certainty. [p.11] 'Studies not available in the English language… were not eligible.' We suggest that exclusion of non-English evidence may disproportionately affect reviews of rare conditions. As noted above, key implementation evidence from Germany, including G-BA documentation from 2023, and other European programmes is not fully captured in English-language literature. As we highlight on p.9 of Time to decide, this approach risks systematically excluding relevant international evidence and contributes to repeated gaps in UK NSC reviews across rare conditions. Further, Genetic Alliance UK frequently meets with researchers in newborn screening in other countries, and many international counterparts to the UK NSC express a high level of willingness to support evidence gathering and help address methodological challenges. We welcome the UK NSC's recent efforts to engage internationally, but query whether this extends to teams commissioned to review evidence for individual conditions, where this would be particularly valuable. [p.11] 'does not include work published elsewhere (grey literature).' We suggest that excluding grey literature may omit critical implementation evidence. For rare conditions, real-world programme data, policy documentation and clinical network outputs are often the primary sources of evidence. As we set out on p.12 of Time to decide, decision-making frameworks should explicitly incorporate real-world and implementation evidence, particularly where formal trial data are limited. [p.14]

			‘these studies were not included… as they did not evaluate DBS or stool colour card screening.’ We suggest that excluding alternative screening approaches, such as direct or conjugated bilirubin pathways, narrows the scope of the review. Emerging US studies have demonstrated promising sensitivity for bilirubin-based screening approaches, as referenced within the review itself, indicating that screening pathways are evolving. As we note on p.9 of Time to decide, horizon scanning should actively support innovation and future pathway development rather than focusing only on established modalities. [p.53] ‘Cost-effectiveness not considered in this evidence summary.’ While we recognise the methodological rationale, cost-effectiveness is highly relevant for a low-cost intervention such as stool colour card screening. Canadian evaluations have assessed cost-effectiveness alongside screening implementation: www.mdpi.com/2077-0383/11/4/999. As we highlight on p.12 of Time to decide, where economic evidence gaps exist, there is a strong case for commissioning modelling or pilots rather than allowing absence of UK-specific analysis to delay progress. [p.59] ‘pilot studies and/or data collection from the first implemented screening programmes are likely to inform future evidence reviews.’ We support this statement but suggest a more proactive UK approach is warranted. A growing number of countries have already implemented screening and are generating real-world evidence. As we conclude on p.15 of our report, the UK should move towards structured pilots or in-service evaluations to actively contribute to the evidence base, rather than waiting for complete certainty before acting. This shift is urgently needed to address growing concerns from our community and network of international stakeholders that the current approach to evidence reviews on a condition-by-condition basis is simply not fit for purpose when it comes to addressing the unmet needs of the 3.5 million or so population of people living in the UK affected by a rare condition.
S2	Dr Lauren Johansen	British Association for the Study of the Liver (BASL)	In accordance with the recommendation of the UK National Screening Committee, we do not recommend that newborn screening for Biliary atresia be introduced in the UK. There is a lack of high-quality evidence demonstrating that either dried blood spot testing or stool colour cards reduce the morbidity or mortality associated with biliary atresia (criterion 11). A small number of published studies have evaluated different

			components within dried blood spots for the diagnosis of biliary atresia, including free carnitine, MMP-7, bile acids, and the metabolites taurohyocholic acid, indoleacetic acid, and 2-hydroxyglutaric acid. The positive predictive value of all tests was low, likely influenced by the low prevalence of the condition. Although the sensitivity of some tests exceeded 90% in certain cases, the confidence intervals were wide. There were no studies demonstrating improved native liver survival in infants with biliary atresia diagnosed through dried blood spot testing. Stool colour charts had a higher level of evidence; however, the sensitivity of the tests varied considerably between studies, and the reported confidence intervals were wide. The reported mean age at Kasai portoenterostomy following screening was 48.2–59.7 days, which is consistent with UK data from 2014–2018 showing a median age at Kasai portoenterostomy of 48 days in the absence of screening. Clinical management in the UK therefore already appears to be comparable to that in healthcare systems using stool colour chart screening programmes. Continued adherence to NICE guidance for the investigation of prolonged jaundice, including prompt measurement of conjugated bilirubin levels and evaluation of stool colour by healthcare professionals, is of utmost importance. Information provided by midwives and health visitors to parents regarding normal stool colour, with reference to the Yellow Alert Campaign leaflets, should continue. Early referral of infants with conjugated jaundice and pale stools to the National Paediatric Liver Units for centralised care will help maintain and further improve outcomes in this important patient group.
S3	Michelle Wilkins	British Liver Trust	The incidence of BA is similar to other congenital conditions for which neonatal screening is standard, such as phenylketonuria or galactosemia. Therefore, we believe it is necessary to have some form of screening to identify this life-threatening condition as soon as possible to ensure timely treatment. (Wildhaber BE, 2025) As an organisation working with parents of BA children, we know that there is still misunderstanding and misdiagnosis of this condition due to a lack of healthcare professional knowledge on prolonged jaundice and the impact of BA on bile flow. In a recent call for evidence from our organisation, 19 examples were provided by BA parents being supported by the charity. They all reported misunderstandings and misinformation in relation to both jaundice detection and stool/urine colour. This uncertainly led to delays

			in diagnosis and their Kasai procedure happening later than is ideal for best outcomes for the baby. This often led to liver transplantation as the only viable option for survival. Some of these cases led to serious incidence investigations. We believe there to be many more with similar experiences as our biggest cohort is BA parents and we often hear that the BA was not diagnosed in a timely fashion even if the Kasai was ultimately deemed to be successful. The UK NSC currently states that: • there is no reliable screening test that would be able to detect the disease within the first week of the baby's life In consultation with Professor Mark Davenport, Kings College Hospital London there is evidence that this is inaccurate and has been since 2011. Sunny Harpavat et al. published a key study from Houston, Texas whereby they looked back at all their infants diagnosed with BA for the first bilirubin blood tests. They then sought the split, and it was clear that there was 100% discrimination if one looked at conjugated (i.e. direct) bilirubin within 48 hours of birth. (Harpavat S F. M., 2011) In relation to the point that: • there is no evidence that screened babies would be able to have surgery at a younger age than unscreened babies We again would refute this based on the fact that clinicians still have to investigate all those that are shown to have raised conjugated bilirubin, and the evidence from Houston who have pioneered a two-stage screening programme that repeats the bloods in the 2nd week of life and this brings the age at Kasai down. (Harpavat S R. T., 2026) (Harpavat S L. P., 2018) (Harpavat S L. P., 2018) (Harpavat S A. S., 2025) We also believe that there are many examples of evidence supporting the introduction of the stool colour card (SCC) as a simple yet effective screening tool enabling parents to identify pale stools in their newborn. Not only could a stool chart be placed in the personal health care record or 'red book', but a step further could be to introduce checking of stool colour within the appropriate section of the screening and routine reviews. Globally, Taiwan province of China pioneered BA screening in the 1990s with the introduction of a stool color card (SCC). This simple yet effective tool enables parents and caregivers to identify pale, acholic stools in their newborns, the hallmark of cholestasis and BA in particular. In Taiwan province of China, the introduction of the SCC led to a notable decrease in the age at which the Kasai operation was performed, with the proportion of infants undergoing surgery before 60

			days of age increasing from 49% before the screening program to 66% afterwards. Moreover, the hospitalization and mortality rates of BA cases in Taiwan province of China significantly declined following the introduction of the SCC screening program. (Lee M, 2016) The programme's success set a benchmark for other countries to later also introduce the SCC nationwide, such as Switzerland, France, Germany and Brazil, or regionally, including Japan, China, Canada, and Egypt. The SCC is available either in paper format, often integrated into the child's personal health booklet, or more recently, as part of mobile smartphone applications. We already have physician backing in the UK for the introduction of the SCC as a cost effective and simple tool which enhances parental knowledge and understanding. In 2020 as part of the UK National Screening Committee annual call for new screening topics, Prof Deirdre Kelly, Birmingham Women's & Children's Hospital; Prof Anil Dhawan, Kings College Hospital; Dr Eirini Kyrana, Leeds Teaching Hospitals NHS Trust; Ms Alison Taylor, Children's Liver Disease Foundation (CLDF) proposed a national screening programme for biliary atresia to educate parents and health care providers to differentiate between normal and abnormal stool colour to ensure early referral to a specialist paediatric liver centre to confirm the diagnosis of biliary atresia and perform corrective surgery. Stool colour cards have been developed by CLDF (now British Liver Trust as the two organisations have merged) and could be reproduced within the Personal Child Health Record (the Red Book). Parents would be educated about the significance of the stool colour and advised to contact their GP/Health Visitor if the colour is abnormal, especially if the child is still jaundiced after 14 days of age (NICE guidance). Some would argue that this can lead to an increase in parental anxiety but in our experience supporting parents affected, this is not the case. In fact, on talking to parents with late presentation of BA due to ineffective HCP intervention, they have consistently asked why they didn't know about BA and why was there nothing in their red book about it. Our Yellow Alert campaign continues to provide the SCC and 'a jaundice in the newborn baby' leaflet for parents and we know that NHS community foundation trusts have made localised decisions to place these in the red book after serious incidence investigations. The SCC could also be formally added to the clinical examination as it is within the carnet de santé in France – stool colour is checked at one week and one month – a simple and effective way to monitor if there is an issue with bile moving to the intestine successfully. The implementation of a nationwide BA screening program in France was not driven by clinicians but by a parent-led initiative. In 2009, a group of parents founded the Association Maladies du Foie depuis l'Enfance (AMFE), advocating for better early detection of BA. After nearly a decade of persistent efforts and appeals to French health

			authorities, their advocacy succeeded, and in 2017, the SCC was officially integrated into the French individual health booklet provided to every family at birth. The Feb 2026 evidence summary has concluded: • the accuracy of stool colour cards to identify biliary atresia is unclear because the available evidence is inconsistent • screening using stool colour cards has improved outcomes for infants with biliary atresia in some countries • recent evidence shows that babies in the UK usually have surgery at around 50 days old. This is about the same age as in countries that use stool colour cards to help spot the condition earlier We believe as discussed above that the time to Kasai continues to be hit and miss in terms of parental experience. This is not acceptable. It may be that there is inconsistent evidence but there therefore should be investment in this area to allow more evidence to be gathered. We would ask why NHS community foundations are placing stool charts and Yellow Alert parent leaflets to ensure parents know about prolonged jaundice and stool colour AFTER there has been a delayed diagnosis leading to late Kasai and ultimately a liver transplant as the only option. As a charity we do not have enough financially to invest in this although we do currently provide all of our Yellow Alert materials free of charge to HCPs and parents who request them. While it is generally accepted that the Kasai surgery should occur before 60 days of age to achieve high rates of bile flow restoration, earlier intervention before 45 days is associated with better long-term native liver survival rates. While infants continue to be missed, and presentation to Kasai is later than the optimum there is a reduced chance of a successful outcome, increasing the earlier need for liver transplantation, a complex, life-threatening, expensive surgery with a lifetime of medication and potential complications. The SCC should be tested as a screening tool in the UK to improve outcomes for babies born with BA and their caregivers. References Harpavat S, A. S. (2025). Guidance for the primary care provider in identifying infants with Biliary Atresia by 2 – 4 weeks of life: clinical report. Pediatrics. Harpavat S, F. M. (2011). Patients with biliary atresia have elevated direct/conjugated levels shortly after birth. Pediatrics, 1428-33. Harpavat S, L. P. (2018). Factors influencing time to diagnosis of Biliary Atresia. Journal of Pediatric Gastroenterology, 850-6.

			Harpavat S, R. T. (2026). A strategy to identify biliary atresia efficiently: A perspective from a Texas Centre. World Journal of Pediatric Surgery. Lee M, C. S. (2016). Infant Stool Color Card Screening Helps Reduce the Hospitalization Rate and Mortality of Biliary Atresia.. Medicine (Baltimore). Wildhaber BE, C. A. (2025). European strategies in the screening of biliary atresia: a scoping review. World Journal of Pediatric Surgery.
S4	Rebecca Byers	Ipsen	Good evening On behalf of Ipsen, I attach our response to the National Screening Committee consultation on newborn screening for biliary atresia (in the original ODT. format, as well as PDF for ease). Could I ask that Ipsen is added to the list of organisations with an interest in biliary atresia for future evidence reviews. We are happy to not be listed on the website as we recognise you link to organisational websites. We look forward to the outcome following the NSC's decision meeting in June. Should you have any questions on the content in our response, we would be very happy to discuss, or connect you with colleagues operating in countries where screening for biliary atresia is already taking place. Thank you for the opportunity to participate. Rebecca Rebecca Byers Head of Government Relations and Policy UK & Ireland

UK National Screening Committee

UK National Screening Committee

Consultation Comments Pro-forma

Newborn screening for biliary atresia

Name:	Rebecca Byers	**Email address:**	XXXX XXXX
Organisation (if appropriate):	Ipsen		
Role:	Head of Government Relations and Policy		
Do you consent to your name being published on the UK NSC website alongside your response?	Yes		

Section and / or page number	**Text or issue to which comments relate**	**Comment** *Please use a new row for each comment and add extra rows as required.*
General	General	Ipsen welcomes the opportunity to comment on the UK National Screening Committee (UK NSC) consultation on newborn screening for biliary atresia (BA). Ipsen strongly supports the objective of improving early detection and outcomes and believes the current evidence base – particularly considering known consequences of delayed diagnosis – supports a more proactive position than the draft conclusion to retain a non-recommendation. BA is a time-critical condition where delayed diagnosis can restrict treatment options and worsen long-term clinical outcomes (Masturina et al., 2025; Harpavat et al., 2018). Outcomes are dependent on early intervention: surgery within 30–45 days improves transplant-free survival, whereas outcomes deteriorate beyond 90–120 days (Masturina et al., 2025). However, in practice, late diagnosis remains common, with some infants referred after 60 days, when disease is already advanced (Durkin et al., 2017). Delayed

		referral is consistently associated with increased fibrosis, poorer surgical outcomes, and higher mortality, highlighting the importance of earlier detection (Masturina et al., 2025; Harpavat et al., 2018). Delays to diagnosis are driven by systemic and clinical challenges. Early BA is difficult to distinguish from common benign jaundice, and recognition relies heavily on subjective assessment. This is further complicated by limitations in detecting jaundice across different skin tones, creating a risk of inequity in diagnosis and delayed referral. As a result, both clinicians and parents risk missing early warning signs, contributing to missed opportunities within a narrow therapeutic window. This issue reflects a broader pattern across liver disease. UK patient group data show that around one in five patients with rare liver conditions are diagnosed 'very late', often after disease progression, with many reporting that early symptoms were not acted on (British Liver Trust, No One Left Behind, 2026). Screening – particularly when embedded within the existing newborn dried blood spot (DBS) programme – offers a practical and equitable solution. It provides a standardised, objective mechanism for early detection, independent of subjective symptom recognition, while also increasing awareness of rare conditions among parents and healthcare professionals. Given the UK's well-established DBS infrastructure, this represents a low-burden opportunity to intervene earlier and reduce avoidable harm. We recognise the UK NSC's rigorous application of appraisal criteria. However, we believe the current review underestimates: • the urgency of late diagnosis; • the need for standardised approaches to reduce diagnostic inequity; • the role of screening in raising awareness of BA; and

		• the limitations of applying evidentiary thresholds (ie RCTs) in rare, rapidly progressive neonatal conditions. Given the severity of BA and the consequence of delayed diagnosis, continued deferral of newborn screening risks perpetuating preventable harm. Ipsen therefore encourages the Committee to reconsider whether the evidence supports, at a minimum, conditional recommendation or piloting of DBS-based screening, rather than maintaining a non-recommendation.
External review pp. 10-11, 32-33	Criterion 4 — There should be a simple, safe, precise and validated screening test Question 1 — What is the accuracy of screening tests to detect biliary atresia in newborns?	**Criterion 4: Test accuracy** The review concludes that no screening test has demonstrated sufficient accuracy in a general newborn screening context, particularly when delivered via dried blood spots (DBS) (pp. 10–11, 32–33). Ipsen agrees that screening using stool colour (SCC) cards and DBS-based screening for biliary atresia (BA) remains an emerging approach, but this may reflect implementation maturity rather than absence of a valid screening test. There is now consistent evidence that direct (conjugated) bilirubin is elevated from birth in infants with BA, supporting its validity as an early screening biomarker (Harpavat et al., 2025). This early biological signal aligns with the timing of newborn DBS sampling, providing a scientific rationale for translation into a population screening programme. The review also acknowledges that bilirubin-based screening approaches demonstrate very high sensitivity (approaching 100%) and specificity (~99.9%) in large real-world cohorts (pp. 15, 32). These data underpin international guidance: • These programmes are explicitly endorsed in the American Academy of Pediatrics (AAP) 2025 Clinical Report, which provides practical

		guidance for universal assessment of jaundice, stool colour and measurement of direct or conjugated bilirubin at 2–4 weeks of life to identify BA before the optimal surgical window is missed (Harpavat et al., 2025). • The AAP guidance is based on population-level evidence (including Harpavat et al., 2020) demonstrating that direct bilirubin is elevated from birth in infants with BA, supporting both its biological plausibility and clinical validity as a screening marker. Taken together, this evidence demonstrates that: • A clinically validated biomarker exists (direct bilirubin); • The biomarker is detectable at or near birth; and • Remaining uncertainty relates to optimising delivery via DBS, rather than test validity itself. In this context, DBS offers a simple, low-cost and scalable platform, building on established national screening infrastructure with high coverage and acceptability to generate UK-specific evidence. It provides a practical opportunity to implement population-level screening now, while reducing reliance on subjective clinical recognition and enabling earlier detection of a time-critical condition. This approach would also provide a foundation for future refinement of screening strategies, including the incorporation of optimised bilirubin-based testing or alternative biomarkers as the evidence base continues to evolve.
External review: pp. 32–33	Criterion 18 and Criterion 22: Feasibility and acceptability	**Criteria 18 and 22: Applicability to the UK setting**

		The review highlights concerns regarding feasibility and follow-up systems for bilirubin testing in a population screening context. Ipsen agrees that robust pathways are essential; however, the UK is well positioned to implement DBS-based screening within existing systems. • The UK already operates a mature, population-wide newborn screening programme using DBS, with established laboratory workflows and follow-up pathways • There is established clinical familiarity with bilirubin testing and management of neonatal jaundice, supporting downstream pathways (Harpavat et al., 2025). • The UK's centralised BA services and referral pathways support timely escalation, which is critical given that delays beyond 60 days are associated with disease progression and poorer outcomes (Masturina et al., 2025; Harpavat et al., 2018). • Alignment with existing scheduled contacts (ie midwife and health visitor checks at 10–14 days and 6–8 weeks) could address logistical concerns. Beyond feasibility, DBS screening provides an objective approach to detection, reducing reliance on recognition of jaundice – which is variable and may be harder to identify across different skin tones – and helping address known delays in rare liver disease diagnosis (British Liver Trust, 2026).
UK NSC External Review, pp. 34–36	Criterion 15 – Clinical management of the condition and patient outcomes should be optimised in all health care providers prior to participation in a screening programme Question 2 – What is the reported age at surgery/time	**Criterion 15: Optimising patient outcomes and clinical management** The review reports a median age at Kasai portoenterostomy in the UK of 51 days, improving to 48 days in the most recent period (2014–2018), and concludes that this is comparable to screened countries.

	to surgery for biliary atresia (Kasai portoenterostomy) in the UK?	Ipsen welcomes the progress achieved in UK BA care and agrees that centralisation has improved outcomes. However, focusing on median age risks overestimating the extent to which outcomes are fully optimised. • Despite a favourable median, a proportion of infants still undergo late surgery (ie >100 days), where outcomes are worse. Delays beyond 60–90 days are associated with reduced liver survival, greater fibrosis, and increased mortality (Masturina et al., 2025). • Median figures do not capture missed or delayed diagnoses, which may arise from early symptoms such as jaundice being attributed to benign causes (Harpavat et al., 2018). • Evidence from other centralised systems (ie Switzerland and Taiwan) shows that screening can reduce the 'tail' of late presenters, even where overall median age is already relatively low (Wildhaber and Calinescu, 2025). These gaps are particularly important given national policy priorities. The UK Rare Disease Action Plan highlights earlier diagnosis and improved identification as key system objectives, recognising that delayed diagnosis leads to poorer outcomes and missed opportunities for intervention (Department of Health and Social Care, 2021).
UK NSC External Review, pp. 37–43	Criterion 11 – Effectiveness of the screening programme There should be evidence from high quality randomised controlled trials that the screening programme is effective in reducing mortality or morbidity	**Criterion 11: Absence of RCTs should not preclude progress** The review concludes that Criterion 11 is not met due to the absence of randomised controlled trials (RCTs). However, Ipsen believes that applying an RCT standard in this context is disproportionately restrictive for a rare, progressive neonatal condition. • No national BA screening programme globally has been evaluated through RCTs, largely because randomisation to delayed or absent diagnosis could

		be ethically and practically challenging, given the known impact of timing on outcomes (Masturina et al., 2025). • Evidence consistently demonstrates that earlier diagnosis leads to improved outcomes, with delays associated with worsening disease, reduced native liver survival and increased mortality (Masturina et al., 2025; Harpavat et al., 2018). • In line with broader newborn screening practice, many established programmes rely on observational, population-based and before-and-after evidence, particularly in rare diseases where RCTs are not feasible (Wildhaber and Calinescu, 2025). Taken together, the evidence base for BA screening reflects real-world effectiveness rather than experimental trial design, which is consistent with precedent in newborn screening policy. A broader interpretation of effectiveness evidence, aligned with established screening practice, would better reflect the realities of rare disease research and support consideration of pilot or phased implementation.
UK NSC External Review, pp. 37–43	Criterion 13 – Benefit and harms from screening programmes The benefit gained by individuals from the screening programme should outweigh any harms, for example from overdiagnosis, overtreatment, false positives, false reassurance, uncertain findings and complications	**Criterion 13: Evidence of benefit, including in Western healthcare systems** The review recognises consistent improvements in time to surgery and outcomes following screening programmes in Japan, Taiwan and China, but expresses uncertainty regarding applicability to Western healthcare systems. While contextual differences should be considered, there is increasing evidence from European settings: • The European scoping review highlights that countries such as Switzerland and France have successfully embedded stool colour card

		(SCC) screening into national child health records, with evidence of earlier referral and improved timing of surgery over time (Wildhaber and Calinescu, 2025). • The same review concludes that combining SCC with bilirubin measurement may offer the most effective and cost-efficient approach for Western healthcare systems (Wildhaber and Calinescu, 2025). • Experience in Germany demonstrates that outcomes are strongly influenced by implementation quality, clinician engagement and parental awareness, rather than intrinsic limitations of screening approaches – supporting the potential use of DBS in the UK (Wildhaber and Calinescu, 2025).
UK NSC External Review, pp. 37–43	Criterion 13 – Benefit and harms from screening programmes The benefit gained by individuals from the screening programme should outweigh any harms, for example from overdiagnosis, overtreatment, false positives, false reassurance, uncertain findings and complications	**Criterion 13: Harms, false positives and system capacity** Ipsen acknowledges the Committee's concerns regarding false positives and the capacity required for follow-up. However, the available evidence indicates these risks are limited and manageable, particularly when considered alongside the consequences of missed or delayed diagnosis. • Reported false-positive rates are low for both stool colour card (SCC) and bilirubin-based screening, typically well below levels seen in many established newborn screening programmes (Wildhaber and Calinescu, 2025). • Early identification of other cholestatic liver diseases, while sometimes classified as "incidental findings", may represent a net clinical benefit, enabling earlier intervention in conditions where treatment is available (Wildhaber and Calinescu, 2025). • Crucially, delayed diagnosis of BA is associated with disease progression, reduced surgical success and increased mortality,

		meaning that missed cases carry substantial and irreversible harm (Masturina et al., 2025; Harpavat et al., 2018). There is growing clinical consensus that for BA, the risks associated with under-diagnosis may outweigh those of cautious over-screening, particularly where follow-up pathways are already established. Embedding screening within a DBS-based programme further mitigates potential harms by providing a standardised, low-burden approach to early detection, reducing reliance on subjective clinical recognition and supporting equitable access.
General	General	Ipsen encourages the UK NSC to consider the following in lieu of a non-recommendation: 1. **Conditional or pilot recommendation:** Progressing a pilot or phased implementation of DBS-based screening would enable real-world evaluation within existing NHS infrastructure, while generating UK-specific evidence on feasibility, performance and outcomes. 2. **Integration into existing child health pathways:** Exploration of integration into the Personal Child Health Record (red book), including stool colour awareness, drawing on models from France and Switzerland (Wildhaber and Calinescu, 2025), to complement biochemical screening and support early recognition. 3. **Clinical and patient engagement:** Engagement with UK stakeholders (e.g. BSPGHAN, British Liver Trust, Children's Liver Disease Foundation) to ensure programme design addresses real-world diagnostic challenges, improves awareness, and minimises parental anxiety (British Liver Trust, 2026).

General	General	Ipsen believes that the balance of current evidence supports a more proactive stance on newborn BA screening in the UK. While uncertainties remain, these are not unique to BA and should be weighed against the seriousness of the condition, the narrow window for effective intervention, and the increasing international consensus around feasible screening approaches. We respectfully encourage the UK NSC to consider whether the current conclusion to retain a non-recommendation remains proportionate, or whether conditional implementation, piloting, or phased adoption would better serve children, their families and the ambitions of the NHS in accelerating earlier diagnosis for rare diseases.

Please return your completed form to the UK NSC Inbox UKNSC@dhsc.gov.uk by 11.59pm on 20 May 2026.