

Developing an ELSI readiness matrix for genomic newborn screening

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Supplementary Table S1. Source-level corpus and critical extraction

Corpus identifiers S01–S60 correspond to references 1–60 in the manuscript.

Note. “Critical limitation” records the principal, but not necessarily exhaustive, source-specific constraint relevant to the interpretation or transferability of each source. It is a narrative, design-sensitive appraisal field and does not constitute a formal quality rating, risk-of-bias assessment or cross-design score. It should be interpreted alongside the source type, design, jurisdiction and maturity of the evidence. Priority reflects the analytical materiality and transferability of a source’s contribution to matrix development; it is not a methodological quality rating and carries no numerical weight.

Source	Design / evidence type	Context and stage	Programme-level contribution	Critical limitation	Priority
S01. Wilson and Jungner (1968) <i>Principles and practice of screening for disease.</i> WHO Public Health Papers No. 34	WHO monograph / foundational screening framework.	General population screening, international, foundational principles.	Establishes condition importance, accepted treatment, diagnostic and treatment facilities, natural history, agreed treatment policy, economic balance and continuing programme review.	Historical report rather than an indexed journal article. Its content is not specific to genomics or ELSI readiness.	Contextual
S02. Andermann et al. (2008) <i>Revisiting Wilson and Jungner in the genomic age: a review of screening criteria over the past 40 years.</i> https://doi.org/10.2471/BLT.07.050112	Review and updated screening principles.	General population screening, international, policy appraisal and programme evaluation.	Updates screening principles to include programme objectives, equity, informed choice, confidentiality, integration, quality assurance and planned evaluation.	Broad screening framework, does not operationalise gNBS-specific data or longitudinal duties.	High
S03. Grosse et al. (2009) <i>Population screening for genetic disorders in the 21st century: evidence, economics, and ethics.</i> https://doi.org/10.1159/000226594	Comparative review of evidence-based screening appraisal.	United States, United Kingdom and the Netherlands. Policy appraisal and pilot decisions.	Shows why benefits, harms, ethics and opportunity costs must be appraised together and why jurisdictions may reasonably reach different conclusions.	Predates contemporary gNBS pilots and large-scale genomic data reuse.	High
S04. Knoppers et al. (2014) <i>Whole-genome sequencing in newborn screening programs.</i> https://doi.org/10.1126/scitranslmed.3008494	Health-policy commentary.	International gNBS policy. Pre-implementation deliberation.	Identifies child best interests, incidental findings, carrier and adult-onset information, consent, recontact, storage, insurability, education and system burden as programme-level issues.	Early commentary without empirical implementation evidence.	Moderate
S05. Knoppers et al. (2025) <i>Genomic sequencing in newborn screening: balancing consent with the right of the asymptomatic at-risk child to be found.</i> https://doi.org/10.1038/s41431-024-01677-w	Normative ethical and legal analysis.	International gNBS research programmes and public-health ethics. Consent model and programme scope.	Develops an ‘appropriate consent’ argument that proportionately balances universal case-finding with genomic complexity and child-centred benefit.	Normative proposal, the proposed right and consent model are not universal legal standards.	High
S06. Downie et al. (2021) <i>Principles of genomic newborn screening programs: a systematic review.</i> https://doi.org/10.1001/jamanetworkopen.2021.14336	Systematic review of evidence-generating gNBS studies.	International, programme design and early implementation	Synthesises evidence on parental uptake, gene selection, validity, utility and ELSI. It supports transparent selection, flexible consent, reduced uncertainty, equitable access and adaptable programmes.	Evidence base ended in April 2021 and was dominated by early research studies rather than routine programmes.	High
S07. Friedman et al. (2017) <i>Genomic newborn screening: public health policy considerations and recommendations.</i> https://doi.org/10.1186/s12920-017-0247-4	Consensus-based policy recommendations.	Global Alliance for Genomics and Health. Pre-implementation policy.	Requires demonstrated clinical utility and cost-effectiveness, reliable variant interpretation, child best interests and jurisdiction-specific policies for findings, storage and sharing.	Consensus recommendations predate current large-scale pilots and recent evidence on data reuse and equity.	High

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S08. Stark and Scott (2023) <i>Genomic newborn screening for rare diseases.</i> https://doi.org/10.1038/s41576-023-00621-w	Narrative review.	International gNBS pilots. Evidence generation and implementation planning.	Integrates actionability, uncertainty, consent, psychosocial effects, privacy, reuse, equity, trust, evidence generation and infrastructure.	Broad narrative review published while large-scale gNBS projects were still launching; it synthesises anticipated opportunities and challenges but cannot establish population-level clinical benefit, harms, cost-effectiveness, implementation performance or long-term psychosocial outcomes.	Moderate
S09. Rahimzadeh et al. (2022) <i>Exome/genome-wide testing in newborn screening: a proportionate path forward.</i> https://doi.org/10.3389/fgene.2022.865400	Normative public-health policy analysis.	International. Scope and staged implementation.	Applies proportionality to require clinical utility, accurate interpretation, cost-effectiveness, universal access and downstream care. Its proposal favours staged or second-tier use where evidence is incomplete.	Normative analysis rather than an empirical test of programme performance.	High
S10. Schnabel-Besson et al. (2026) <i>A multi-dimensional framework for establishing and managing a genomic newborn screening program.</i> https://doi.org/10.1038/s41431-026-02045-6	Interdisciplinary consensus framework.	Germany. Intended international application, condition selection and programme management.	Operationalises clinical, diagnostic, therapeutic-interventional and programme-management criteria through a structured consensus process including patient representatives.	Consensus framework, independent application and empirical validation remain needed.	High
S11. Freeman et al. (2025) <i>Evaluating whole genome sequencing for rare diseases in newborn screening: evidence synthesis from a series of systematic reviews.</i> https://doi.org/10.3310/DJRF1124	Health technology assessment and linked systematic reviews.	United Kingdom. International evidence, evidence appraisal for policy.	Finds major gaps in population penetrance, expressivity, diagnostic accuracy, effectiveness and economic evidence. Its content demonstrates limits of transferring clinical evidence to genotype-first screening.	Detailed review of selected conditions and methods. This review does not resolve how every proposed gNBS condition should be appraised.	High
S12. Howard et al. (2015) <i>Whole-genome sequencing in newborn screening? A statement on the continued importance of targeted approaches in newborn screening programmes.</i> https://doi.org/10.1038/ejhg.2014.289	Professional policy statement.	European and international professional bodies. Programme scope and reporting policy.	Defends targeted analysis for high-risk, preventable or treatable early-onset conditions and specifies limits on findings, consent, data and system obligations.	Predates contemporary gNBS implementation studies and evolving treatment landscapes.	Moderate
S13. Milko et al. (2019) <i>An age-based framework for evaluating genome-scale sequencing results in newborn screening.</i> https://doi.org/10.1016/j.jpeds.2018.12.027	Method-development study.	United States. NC NEXUS. Gene-disease and result selection.	Provides a semi-quantitative age-based actionability metric and demonstrates classification of 822 gene-disease pairs.	Actionability scoring supports result selection but does not by itself establish programme-level readiness or child-centred net benefit.	Moderate
S14. Brown et al. (2026) <i>Genomic newborn screening: a scoping review of the field's evolution and associated ethical, legal, and social implications.</i> https://doi.org/10.1038/s41431-026-02108-8	Large scoping review with AI-assisted charting.	International. This review includes 485 publications, cross-stage evidence and gap mapping.	Maps 3,781 ELSI considerations to 59 decision points and shows that long-term stewardship, follow-up and sustainable governance are underexplored.	Maps the field rather than validating a readiness instrument.	High
S15. Jungkunz and Schickhardt (2025) <i>Ethics of genomic newborn screening - a child centered public health framework.</i> https://doi.org/10.1007/s00481-025-00867-4	Systematic normative framework development.	International public-health ethics. Ethical appraisal of programme design.	Derives child-centred public-health norms and links gNBS to health, family welfare and autonomy within a substantive best-interests account.	Normative synthesis, does not supply measurable readiness thresholds or implementation outcomes.	High

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S16. Settegast et al. (2025a) <i>Towards genomic newborn screening, part I: mapping the ethical issues.</i> https://doi.org/10.1007/s00481-025-00884-3	Integrative ethical review.	International. Programme design.	Maps target selection, uncertainty, consent, counselling, data generation, storage and use, and proposes child-centred constraints on programme scope.	Conceptual mapping without empirical validation or jurisdiction-specific legal analysis.	High
S17. Settegast et al. (2025b) <i>Towards genomic newborn screening, part II: outlining a normative framework.</i> https://doi.org/10.1007/s00481-025-00885-2	Integrative review and normative framework.	International. Programme design and parental authorisation.	Specifies parental duties, children's privacy, informational self-determination, the right not to know, the child's open future and best interests; it also addresses medicalisation..	Normative framework. Contested principles require jurisdiction- and context-sensitive application.	High
S18. Watts et al. (2025) <i>Three ethical approaches to expanding newborn screening through genomics: a critical comparative analysis.</i> https://doi.org/10.1186/s12910-025-01331-0	Comparative normative analysis.	International. Policy framing.	Compares liberal individualism, public-health ethics and genomic-health-rights approaches and argues for public-health ethics with protections against state or parental overreach.	Normative analysis. This analysis does not establish empirical readiness criteria.	High
S19. Pichini et al. (2022) <i>Developing a national newborn genomes program: an approach driven by ethics, engagement and co-design.</i> https://doi.org/10.3389/fgene.2022.866168	Implementation design paper.	England. Newborn Genomes Programme. Pre-implementation co-design.	Shows how ethics, public dialogue, co-design, condition selection, consent, data use and sustainability can be embedded prospectively.	Describes programme design before outcome data were available.	High
S20. Etheredge et al. (2026) <i>Embedding ethics into Genomics England's Generation Study.</i> https://doi.org/10.1136/bmjopen-2025-112134	Programme ethics analysis / communication.	England. Generation study. Implementation.	Operationalises embedded ethics through an ethics group, public dialogue, design research, transparency, uncertainty management, treatment pathways, storage and access rules.	Single research programme. It describes governance processes more than comparative outcomes.	High
S21. Reimers et al. (2025) <i>Clinical utility and cost-effectiveness of BeginNGS newborn screening by genome sequencing and standard newborn screening for severe childhood genetic diseases: an adaptive, international and comparative clinical trial.</i> https://doi.org/10.1136/bmjopen-2024-098609	Adaptive multicentre clinical trial protocol.	International. BeginNGS. Evidence-generating implementation.	Pre-specifies adaptive disease qualification, multilingual consent, return of results, counselling, confirmation, treatment guidance, clinical utility and cost-effectiveness outcomes.	Protocol rather than results. It proposed outcomes cannot yet be treated as demonstrated programme readiness.	Moderate
S22. Ziegler and Chung (2025) <i>Universal newborn screening using genome sequencing: early experience from the GUARDIAN study.</i> https://doi.org/10.1038/s41390-024-03647-w	Narrative review of early programme experience.	United States. GUARDIAN and international pilots. Early implementation.	Connects initial GUARDIAN experience with acceptability, equity, scalability, dried-blood-spot workflows and downstream clinical infrastructure.	Early experience and narrative comparison. This review cannot establish long-term benefit or sustainability.	Moderate
S23. VanNoy et al. (2019) <i>Challenging the current recommendations for carrier testing in children.</i> https://doi.org/10.1542/peds.2018-1099F	Ethical and clinical commentary informed by BabySeq.	United States. BabySeq. Return-of-results policy.	Examines benefits, harms and autonomy implications of returning carrier status to parents and clinicians.	Narrow focus on carrier findings. Its content does not assess whole-programme readiness.	Moderate

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S24. O'Rourke et al. (2020) <i>The new definition of health technology assessment: a milestone in international collaboration.</i> https://doi.org/10.1017/S0266462320000215	International consensus definition of HTA.	International. Comparative policy appraisal.	Confirms that HTA already considers clinical, economic, organisational, social, ethical and legal consequences through multidisciplinary processes.	Not specific to newborn or genomic screening. This paper functions as a comparator rather than direct gNBS evidence.	High
S25. Erazo and González-Lamuño (2026) <i>Cribado neonatal en España: equidad, valor clínico y retos ante la expansión tecnológica.</i> (in press)	Narrative review manuscript.	Spain. Policy context and expansion.	Synthesises territorial equity, governance, proportionality, clinical value and health-system capacity challenges in Spanish NBS expansion.	Historical narrative review with relevance-based source selection. Its conclusions are time-sensitive as Spanish programmes and regulations evolve.	Contextual
S26. Phillips et al. (2026) <i>What do we mean by actionability? Examining a key criterion in genomic prenatal and newborn screening.</i> https://doi.org/10.1016/j.gim.2025.101624	Conceptual commentary.	Genomic prenatal and newborn screening. Condition and result selection.	Separates actionability from severity, penetrance, expressivity, utility and treatment burden, showing why the concept cannot serve as a single inclusion threshold.	Conceptual analysis without empirical thresholds or programme validation.	High
S27. Goddard et al. (2022) <i>Establishing the medical actionability of genomic variants.</i> https://doi.org/10.1146/annurev-genom-111021-032401	Narrative review and conceptual synthesis of medical actionability.	Genomic medicine across the life course, including population and newborn screening. Condition and result selection.	Distinguishes medical actionability from clinical utility and supports transparent appraisal of severity, likelihood, intervention effectiveness, burden and evidence quality across individual, family and societal benefits.	Broad genomic-medicine review rather than a gNBS-specific programme evaluation. Actionability is only one component of readiness and does not establish net benefit, cost-effectiveness or implementation feasibility.	High
S28. Kleiderman et al. (2025) <i>Unpacking the notion of “serious” genetic conditions: towards implementation in reproductive decision-making?</i> https://doi.org/10.1038/s41431-024-01681-0	Conceptual framework informed by a rapid review and an international interdisciplinary workshop.	Reproductive genomics in clinical care and population health. Policy deliberation and condition selection.	Frames seriousness as value-laden and context-dependent and integrates medical criteria, treatment and support access, lived experience, procedural fairness, shared decision-making and provider training.	Developed primarily for reproductive decision-making rather than gNBS. The rapid-review- and workshop-informed framework has not been prospectively applied or empirically validated.	High
S29. Armstrong et al. (2022) <i>Parental attitudes toward standard newborn screening and newborn genomic sequencing: findings from the BabySeq Study.</i> https://doi.org/10.3389/fgene.2022.867371	Empirical parental survey.	United States. BabySeq. Post-result attitudes and consent preferences.	Shows stronger support for universal standard NBS than nGS and greater support for explicit consent for nGS.	Research participants were self-selected and may not represent population-level uptake or marginalised groups.	Moderate
S30. Joseph et al. (2016) <i>Parental views on expanded newborn screening using whole-genome sequencing.</i> https://doi.org/10.1542/peds.2015-3731H	Qualitative focus-group study.	United States. Socioeconomically and ethnically diverse parents. Programme design.	Documents demand for inclusion, informed consent, control over results and storage, and the role of limited institutional trust in diverse groups.	Small qualitative sample and hypothetical scenario. Findings are context-specific.	High
S31. Lynch et al. (2024) <i>Australian public perspectives on genomic newborn screening: risks, benefits, and preferences for implementation.</i> https://doi.org/10.3390/ijns10010006	Qualitative public focus-group study.	Australia. Pre-implementation service design.	Shows conditional support, prioritisation of early diagnosis and treatment, and preference for antenatal information.	English-speaking volunteer sample recruited through social media. This study does not establish population acceptability.	Moderate

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S32. Tarini and Goldenberg (2012) <i>Ethical issues with newborn screening in the genomics era.</i> https://doi.org/10.1146/annurev-genom-090711-163741	Narrative ethical review.	United States and international literature. Early policy anticipation.	Anticipates how genomics magnifies consent, information, privacy, storage, results, evidence and programme-capacity challenges in NBS.	Predates current gNBS technology, pilots and regulatory developments.	Contextual
S33. Lewis et al. (2026) <i>Genomic newborn screening: data retention for research and clinical reuse.</i> https://doi.org/10.1038/s41431-026-02120-y	Policy-oriented ethical and legal analysis.	International. Jurisdiction-sensitive. Long-term data stewardship.	Distinguishes retention for research, quality assurance/quality improvement, updating aggregated databases and clinical reuse, and argues for purpose-specific permission, duration and recontact arrangements.	Focuses primarily on genomic data. Residual biological specimens require additional specimen-specific sources and law.	High
S34. Potter et al. (2015) <i>Education and parental involvement in decision-making about newborn screening: understanding goals to clarify content.</i> https://doi.org/10.1007/s10897-014-9780-x	Conceptual education framework.	Canada and comparative NBS models. Information and parental decision-making.	Links educational goals and content to different participation models and supports comprehensive, flexible information even when parents do not make an active choice.	Traditional NBS focus. Genomic complexity and digital consent require additional evidence.	High
S35. Tluczek et al. (2022) <i>Psychosocial issues related to newborn screening: a systematic review and synthesis.</i> https://doi.org/10.3390/ijns8040053	Systematic review of 92 empirical studies.	International NBS; Results communication and long-term family impact.	Synthesises parental knowledge, responses, communication, carrier findings, family burden and disparities. Identifies education, counselling and developmental guidance as mitigations.	Most included studies concern traditional NBS. Genomic findings may intensify or alter psychosocial effects.	High
S36. Parfett et al. (2024) <i>Views of children and young adults about whole genome sequencing in newborn screening: a qualitative study.</i> https://doi.org/10.1038/s41431-024-01614-x	Qualitative study with children and young adults.	United Kingdom; Design, result policy and later consent.	Provides direct evidence on children's and young adults' understanding, concerns, result preferences and expectations for involvement in decisions.	Small purposive samples, including children with cystic fibrosis. Transferability to healthy populations is limited.	High
S37. Zacharias et al. (2018) <i>The legal dimensions of genomic sequencing in newborn screening.</i> https://doi.org/10.1002/hast.884	Legal analysis.	United States. Mandate, consent, access and privacy policy.	Shows why the legal basis for mandatory NBS weakens as scope expands beyond serious immediate harm and analyses refusal, access to raw data and privacy implications.	US-specific law. Rights and duties cannot be generalised across jurisdictions.	High
S38. Preslan and Mathews (2013) <i>A comparative analysis of the governance and use of residual dried blood spots from state newborn screening programs and neonatal biobanks.</i> https://doi.org/10.1525/jer.2013.8.3.22	Comparative governance content analysis.	United States. Residual sample governance and research use.	Empirically documents variation in permissible research, review criteria and governance of residual dried blood spots.	Predates gNBS and is limited to US programmes and sample-based governance.	Moderate
S39. Rahimzadeh et al. (2020) <i>Ethical, legal, and social issues of responsible data sharing involving children in genomics: a systematic review and implications for policy.</i> https://doi.org/10.1080/23294515.2020.1818875	Modified systematic review of reasons and policies.	International paediatric genomics. Data sharing and longitudinal governance.	Identifies benefits, privacy risks and conditions for responsible sharing, including recontact and recontact at the age of majority.	Paediatric genomics rather than NBS-specific. Consent requirements remain law- and programme-dependent.	High
S40. Ersig et al. (2023) <i>Call to action for advancing equitable genomic newborn screening.</i> https://doi.org/10.1159/000534648	Equity-focused perspective.	International with attention to low-resource settings. Programme design and scale-up.	Argues that detection is not equivalent to outcome equity and highlights treatment access, trust, privacy, psychosocial harms and global resource disparities.	Perspective article without a systematic or empirical equity evaluation.	High

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S41. Petrou and Ormond (2025) <i>Equity in newborn sequencing: a capability approach perspective.</i> https://doi.org/10.1007/s00481-025-00882-5	Normative equity analysis.	International. Programme design and downstream care.	Shows that universal offer alone does not create equity and specifies capabilities needed to understand, choose, access and translate findings into health outcomes.	Conceptual framework. The proposed capabilities require empirical indicators and local adaptation.	High
S42. Scarfe et al. (2025) <i>'Jumping too far ahead': Australian healthcare professional, scientist, and policy maker perspectives on using genomics in newborn screening.</i> https://doi.org/10.1038/s41431-025-01954-2	Qualitative stakeholder study.	Australia; federated NBS system. Pre-implementation readiness.	Provides direct empirical support for national coordination, consent, reporting policy, workforce, laboratory and data infrastructure, downstream services and agreed data uses.	Australian stakeholder sample. Views identify requirements but do not measure whether systems meet them.	High
S43. Pàmpols Ros et al. (2022) <i>Cribado neonatal genómico. Perspectiva de la Comisión de Ética de la Asociación Española de Genética Humana. Parte II: aspectos éticos, legales y sociales (AELS) de la introducción de las tecnologías de secuenciación masiva (NGS) en un programa de cribado.</i> https://ojs.sanidad.gob.es/index.php/resp/article/view/269	Spanish professional ethics perspective.	Spain. Pre-implementation policy.	Supports targeted rather than unrestricted sequencing, best interests, proportionality, empirical appraisal, costs and public consensus within Spanish NBS.	Professional perspective rather than empirical assessment. Programme and legal context continue to evolve. Its conclusions are time-sensitive as Spanish programmes and regulations evolve.	High
S44. García-Villoria et al. (2026) <i>The Spanish Uniform Newborn Screening Panel (SUSP): a national consensus framework for harmonized newborn screening.</i> https://doi.org/10.3390/ijns12030067	National multidisciplinary consensus and programme-level harmonisation framework	Spain. Conventional newborn screening; national harmonisation framework within a decentralised health system.	Provides an operational example of nationwide professional consensus, standardised nomenclature and harmonised confirmatory diagnostic pathways intended to reduce regional variation and promote equitable newborn screening across autonomous communities.	Addresses conventional biomarker-based newborn screening rather than gNBS and does not empirically evaluate genomic implementation or the proposed matrix. Its relevance to gNBS is therefore organisational and transferable rather than directly genomic.	High
S45. Dragojlovic et al. (2020) <i>The composition and capacity of the clinical genetics workforce in high-income countries: a scoping review.</i> https://doi.org/10.1038/s41436-020-0825-2	Scoping review of workforce evidence.	High-income countries. Clinical genetics. Capacity planning.	Documents shortages, uncertain scopes of practice and options for task-sharing, alternative service models, process redesign and automation.	Not gNBS-specific and mainly high-income settings. This article does not quantify the incremental workload of population gNBS.	High
S46. Smith et al. (2026) <i>Health economic evaluations of genomic newborn screening: approaches by studies within the International Consortium on Newborn Sequencing.</i> https://doi.org/10.1038/s41431-026-02136-4	International methods survey and reporting recommendations.	International Consortium on Newborn Sequencing. Economic evaluation design.	Identifies current cost-effectiveness and cost-utility plans and recommends transparent reporting of identification, pathways, health outcomes and costs.	Survey captures self-reported plans from 12 ICoNS projects (48% of active projects in August 2024), not completed economic evaluations. Later projects are absent, measures are heterogeneous, and short follow-up leaves lifetime value estimates highly model-dependent.	High

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S47. Kariyawasam et al. (2024) <i>'Integrating ethics and equity with economics and effectiveness for newborn screening in the genomic age: a qualitative study protocol of stakeholder perspectives.</i> https://doi.org/10.1371/journal.pone.0299336	Qualitative study protocol.	Australia. Pre-implementation stakeholder research.	Defines a broad stakeholder design linking ELSI, equity, economics, effectiveness and HTA-informed policy.	Protocol with no empirical findings; planned purposive and network-based sampling within Australia may limit representativeness and transferability, while the qualitative design cannot establish implementation effectiveness or economic outcomes.	Moderate
S48. Wilson et al. (2019) <i>The decision to discontinue screening for carnitine uptake disorder in New Zealand.</i> https://doi.org/10.1002/jimd.12030	Programme reassessment case study.	New Zealand NBS. Post-implementation reassessment and discontinuation.	Shows how low sensitivity and predictive value, uncertain disease burden and treatment harms can justify discontinuing a screened condition through governance review.	Single biochemical NBS condition. Indirect evidence for gNBS but highly relevant to stop rules.	High
S49. Ross and Ormond (2025) <i>Newborn sequencing: the promise and perils.</i> https://doi.org/10.1146/annurev-genom-121123-115349	Narrative review.	United States and international. Policy appraisal and implementation.	Balances diagnostic promise against overdiagnosis, surveillance, treatment and psychosocial harms, consent tensions, inequity and system consequences.	Narrative synthesis. Recommendations require operational testing and jurisdictional adaptation.	High
S50. Lewis et al. (2026) <i>Navigating ethical, legal and social implications in genomic newborn screening.</i> https://doi.org/10.1038/s41576-026-00936-4	Brief policy comment.	GA4GH gNBS working group. international. Implementation policy tools.	Explicitly calls for public-health ethics frameworks and practical tools to navigate strategic ELSI questions during gNBS implementation.	Brief expert Comment presenting a GA4GH policy tool whose 59 decision points were derived from a scoping review. It reports no prospective application or formal end-user evaluation and cannot establish effects on decision quality or implementation outcomes.	Moderate
S51. Ververi et al. (2026) <i>Introducing whole genome sequencing in newborn screening in Greece: ethical, clinical, and policy considerations in the European context.</i> https://doi.org/10.1038/s41431-026-02026-9	Policy comment and governance case.	Greece and European policy. Pre-implementation contracting and public accountability.	Illustrates risks of confidential public-private agreements involving newborn genomes, including authority, transparency, consent, data governance, equity and public trust.	Case-based Comment on a contested Greek agreement, not an evaluation of an implemented screening programme. It reports no participant, clinical, psychosocial, economic or equity outcomes, so its transferability concerns governance principles rather than programme performance.	Moderate
S52. Knoppers et al. (2026) <i>Imagining genomics and population health in 2050: anticipating future research, policy, and governance needs.</i> https://doi.org/10.1159/000552755	Futures and governance analysis.	International population health genomics. Anticipatory governance.	Highlights data abundance, infrastructure, stewardship, AI, regulation, sustainability and global equity as prospective governance needs.	Not specific to gNBS and deliberately prospective; best used in discussion rather than as primary evidence for a matrix element.	Contextual
S53. Couce et al. (2025) <i>Current situation and new steps in newborn screening in Spain.</i> https://doi.org/10.1016/j.anpede.2025.503775	Clinical and policy review.	Spain. Current programme expansion and future gNBS.	Documents recent Spanish NBS expansion, second-tier testing, clinical pathways and emerging genomic initiatives.	Descriptive overview. This review does not systematically evaluate territorial readiness or the proposed matrix.	Contextual

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S54. Leblond et al. (2024) <i>Co-creating the experience of consent for newborn genome sequencing: the Generation Study.</i> https://doi.org/10.1159/000541935	Iterative design research with parents.	England. Generation Study. Consent design and recruitment.	Empirically identifies barriers and enablers across awareness, consideration and informed decision-making and demonstrates iterative co-creation of materials and processes.	Research-study consent in one health system. Implementation choices may not transfer unchanged to routine screening.	High
S55. Lunke et al. (2025) <i>Feasibility, acceptability and clinical outcomes of the BabyScreen+ genomic newborn screening study.</i> https://doi.org/10.1038/s41591-025-03986-z	Prospective cohort study.	Victoria, Australia, 1,000 newborns. Pilot implementation and outcomes.	Demonstrates accredited dried-blood-spot WGS feasibility, turnaround, high-chance findings, clinical actions, cascade diagnoses and high participant acceptability.	Selected research cohort. Short-term pilot outcomes do not establish population effectiveness, equity, opportunity costs or long-term sustainability.	High
S56. Lunke et al. (2024) <i>Prospective cohort study of genomic newborn screening: BabyScreen+ pilot study protocol.</i> https://doi.org/10.1136/bmjopen-2023-081426	Prospective cohort protocol.	Victoria, Australia. BabyScreen+. Pre-implementation and pilot design.	Specifies antenatal recruitment, interpreter access, education, consent, accredited WGS, multidisciplinary evaluation and planned equity and health-economic analyses.	Protocol only; no outcome data were available to assess implementation performance.	Moderate
S57. Kanga-Parabia et al. (2026) <i>How parents decide whether to have genomic newborn screening: experiences from BabyScreen+.</i> https://doi.org/10.1038/s41431-026-02159-x	Mixed-methods parental decision study.	Victoria, Australia. BabyScreen+. Consent and decision-making.	Shows how perceived benefits, severity, barriers, self-efficacy, data concerns and sociodemographic factors shape real parental decisions. It supports tailored and equitable consent.	Participants considered a voluntary research model and may differ from the general population or routine NBS users.	High
S58. Ziegler et al. (2025) <i>Expanded newborn screening using genome sequencing for early actionable conditions.</i> https://doi.org/10.1001/jama.2024.19662	Prospective multicentre observational study.	New York, United States. GUARDIAN interim cohort of 4,000 newborns. Pilot implementation and interim outcomes.	Demonstrates opt-in acceptance in a diverse cohort, sequencing completion and screen-positive yield for a pre-defined panel of early actionable conditions.	Interim non-comparative results demonstrate feasibility, not improved health outcomes, population effectiveness, system readiness or long-term equity.	High
S59. Miller et al. (2015) <i>Governing population screening in an age of expansion: the case of newborn screening.</i> https://doi.org/10.17269/CJPH.106.4897	Cross-jurisdictional governance commentary.	United States, United Kingdom, New Zealand and Canada; Governance of programme expansion.	Compares governance roles and interest coalitions and calls for formal structures balanced in resources and perspectives, with mandates for quality, fairness and accountability.	Predates current gNBS programmes and is a commentary rather than an empirical governance evaluation.	High
S60. Turnbull et al. (2024) <i>Population screening requires robust evidence—genomics is no exception.</i> https://doi.org/10.1016/S0140-6736(23)02295-X	Evidence-focused viewpoint.	United Kingdom population genomic screening. Policy appraisal before scale-up.	Explains why clinically ascertained penetrance and diagnostic-test performance cannot be assumed in asymptomatic populations and calls for robust outcome and economic evaluation.	Viewpoint covering population genomic screening broadly. It does not prescribe a complete gNBS readiness process.	High

Supplementary Table S2. Source-to-domain and source-to-item traceability matrix, with core-source designation

Note. *P=* indicates a primary contribution, where a source directly defines, justifies or operationalises a coded item. *S=* indicates a supporting contribution, where a source corroborates or contextualises it. Codes correspond to Table 1. A blank D1–D6 cell means that the source was not relied upon for that domain.

Core domain(s)= identifies the domain or domains for which a source made a direct and distinctive contribution and was selected as a core source. A blank “Core domain(s)” cell means that the source was not designated as core. Core designation is selective and non-exhaustive and does not constitute a quality rating.

Priority categories carry no numerical weight.

Corpus source	D1. Governance and decision-making architecture	D2. Child-centred justification and proportionality	D3. Consent, information and communication	D4. Genomic data, residual samples and privacy governance	D5. Structural equity	D6. Clinical, organisational and economic capacity	Core domain(s)	Priority
S01. Wilson and Jungner (1968)	S 1.2	P 2.1, 2.2				P 6.2, 6.3, 6.4		Contextual
S02. Andermann et al. (2008)	P 1.1, 1.2	S 2.3	P 3.2		P 5.1	P 6.4; S 6.2		High
S03. Grosse et al. (2009)	P 1.2	P 2.3, 2.4				P 6.3; S 6.4		High
S04. Knoppers et al. (2014)		P 2.3	P 3.2, 3.4	P 4.1, 4.4		S 6.2, 6.3		Moderate
S05. Knoppers et al. (2025)	S 1.1	P 2.3	P 3.2, 3.3; S 3.1				D3	High
S06. Downie et al. (2021)	P 1.2	P 2.1, 2.2	P 3.1, 3.2	S 4.1	P 5.1	S 6.2, 6.4		High
S07. Friedman et al. (2017)	P 1.1	P 2.2, 2.3		P 4.1, 4.2	S 5.1	P 6.3; S 6.2		High
S08. Stark and Scott (2023)	S 1.2	P 2.2, 2.4	P 3.2	P 4.1	P 5.4	P 6.1; S 6.2		Moderate
S09. Rahimzadeh et al. (2022)		P 2.2, 2.3, 2.4			P 5.1, 5.3	P 6.3; S 6.2, 6.4	D2	High
S10. Schnabel-Besson et al. (2026)	P 1.2; S 1.3	P 2.1, 2.2, 2.3	P 3.2		P 5.3	P 6.2, 6.4; S 6.3	D2	High
S11. Freeman et al. (2025)	S 1.2	P 2.1, 2.2, 2.3, 2.4			S 5.2	P 6.3; S 6.4	D2, D6	High
S12. Howard et al. (2015)		P 2.1, 2.2, 2.3	P 3.3	S 4.1		S 6.2		Moderate
S13. Milko et al. (2019)		P 2.1, 2.2	S 3.4					Moderate
S14. Brown et al. (2026)	P 1.2, 1.4	S 2.2	P 3.2	P 4.4	P 5.4	P 6.4; S 6.2, 6.3	D1, D5	High
S15. Jungkunz and Schickhardt (2025)	S 1.3	P 2.3, 2.4	P 3.2, 3.4		S 5.4			High
S16. Settegast et al. (2025a)		P 2.1, 2.2, 2.4	P 3.1, 3.2; S 3.3	P 4.1, 4.2; S 4.3				High
S17. Settegast et al. (2025b)		P 2.3, 2.4	P 3.2, 3.4	P 4.3; S 4.2				High
S18. Watts et al. (2025)	P 1.1	P 2.3	P 3.2, 3.4		S 5.4			High
S19. Pichini et al. (2022)	P 1.3		P 3.1, 3.2	P 4.1	P 5.1	S 6.3, 6.4		High
S20. Etheredge et al. (2026)	P 1.3, 1.4		P 3.1, 3.2	P 4.2	P 5.4	S 6.2, 6.4	D1, D4	High
S21. Reimers et al. (2025)		P 2.2	P 3.1, 3.2		P 5.1	P 6.2, 6.3; S 6.4		Moderate
S22. Ziegler and Chung (2025)		S 2.2	S 3.2		P 5.1	P 6.1, 6.2		Moderate
S23. VanNoy et al. (2019)		P 2.4	P 3.4; S 3.3					Moderate
S24. O'Rourke et al. (2020)	P 1.2; S 1.3	P 2.4			S 5.4	P 6.3		High

Corpus source	D1. Governance and decision-making architecture	D2. Child-centred justification and proportionality	D3. Consent, information and communication	D4. Genomic data, residual samples and privacy governance	D5. Structural equity	D6. Clinical, organisational and economic capacity	Core domain(s)	Priority
S25. Erazo and González-Lamuño (2026)	P 1.1	P 2.3			P 5.3	P 6.2; S 6.3, 6.4		Contextual
S26. Phillips et al. (2026)		P 2.1, 2.2, 2.3, 2.4					D2	High
S27. Goddard et al. (2022)	S 1.2	P 2.1, 2.2, 2.4; S 2.3	P 3.1; S 3.2		S 5.2	S 6.2, 6.4	D2	High
S28. Kleiderman et al. (2025)	P 1.3; S 1.2	P 2.1, 2.3, 2.4; S 2.2			P 5.3, 5.4; S 5.1	P 6.2; S 6.3	D2	High
S29. Armstrong et al. (2022)			P 3.2, 3.4		S 5.1			Moderate
S30. Joseph et al. (2016)	P 1.3		P 3.1, 3.2	P 4.2	P 5.4; S 5.1			High
S31. Lynch et al. (2024)		P 2.3	P 3.1, 3.2		S 5.1			Moderate
S32. Tarini and Goldenberg (2012)	S 1.2		P 3.1, 3.2	P 4.1, 4.2		S 6.2		Contextual
S33. Lewis et al. (2026)	S 1.1		P 3.3	P 4.1, 4.2, 4.3, 4.4			D4	High
S34. Potter et al. (2015)			P 3.1, 3.2		S 5.1		D3	High
S35. Tluczek et al. (2022)		P 2.4	P 3.1, 3.4		P 5.1, 5.4	S 6.2	D3	High
S36. Parfett et al. (2024)		S 2.3	P 3.1, 3.4	P 4.3; S 4.2				High
S37. Zacharias et al. (2018)	P 1.1		P 3.2	P 4.2, 4.3	S 5.1		D4	High
S38. Preslan and Mathews (2013)	P 1.1, 1.2		S 3.3	P 4.1, 4.2				Moderate
S39. Rahimzadeh et al. (2020)			S 3.4	P 4.2, 4.3, 4.4			D4	High
S40. Ersig et al. (2023)			S 3.1	S 4.2	P 5.1, 5.3, 5.4	S 6.3	D5	High
S41. Petrou and Ormond (2025)			S 3.1		P 5.1, 5.2, 5.3, 5.4	S 6.2	D5	High
S42. Scarfe et al. (2025)	P 1.1, 1.2		P 3.2	P 4.2	P 5.3; S 5.4	P 6.1, 6.2; S 6.3	D1, D5, D6	High
S43. Pàmpols Ros et al. (2022)	P 1.2, 1.3	P 2.1, 2.2, 2.3	S 3.2		S 5.4	P 6.3		High
S44. García-Villoria et al. (2026)	S 1.1, 1.2				P 5.3	S 6.2		High
S45. Dragojlovic et al. (2020)			S 3.4			P 6.2, 6.3	D6	High
S46. Smith et al. (2026)		S 2.3				P 6.2, 6.3; S 6.4	D6	High
S47. Kariyawasam et al. (2024)	P 1.3	P 2.4	S 3.2		P 5.4	P 6.3		Moderate
S48. Wilson et al. (2019)	P 1.4	P 2.1, 2.2, 2.4				P 6.4; S 6.2	D6	High
S49. Ross and Ormond (2025)		P 2.3, 2.4	P 3.2		P 5.3; S 5.4	P 6.2; S 6.3		High
S50. Lewis et al. (2026)	P 1.2, 1.4	S 2.3	S 3.2	S 4.2	S 5.4			Moderate
S51. Ververi et al. (2026)	P 1.1, 1.3		S 3.2	P 4.1, 4.2	P 5.4; S 5.1			Moderate
S52. Knoppers et al. (2026)	P 1.4			P 4.2	S 5.2, 5.4	P 6.1; S 6.3		Contextual
S53. Couce et al. (2025)	P 1.1				P 5.3	P 6.2; S 6.1, 6.4		Contextual

Corpus source	D1. Governance and decision-making architecture	D2. Child-centred justification and proportionality	D3. Consent, information and communication	D4. Genomic data, residual samples and privacy governance	D5. Structural equity	D6. Clinical, organisational and economic capacity	Core domain(s)	Priority
S54. Leblond et al. (2024)	P 1.3		P 3.1, 3.2; S 3.3		P 5.1; S 5.4		D3	High
S55. Lunke et al. (2025)		P 2.2, 2.3	S 3.2	S 4.1	S 5.1, 5.3	P 6.1, 6.2		High
S56. Lunke et al. (2024)			P 3.1, 3.2	S 4.1	P 5.1	P 6.1; S 6.3, 6.4		Moderate
S57. Kanga-Parabia et al. (2026)		S 2.1, 2.3	P 3.1, 3.2	S 4.2	P 5.1, 5.4		D3, D5	High
S58. Ziegler et al. (2025)		P 2.2	S 3.2		P 5.1; S 5.2	P 6.1; S 6.2		High
S59. Miller et al. (2015)	P 1.1, 1.2, 1.3, 1.4				S 5.4	S 6.4	D1	High
S60. Turnbull et al. (2024)	S 1.2	P 2.1, 2.2, 2.3				P 6.3; S 6.4	D2	High

Supplementary Table S3. Non-scoring template for prospective application of the ELSI Readiness Matrix

Complete the template for one defined decision and programme stage. Record the matrix version and the evidence corpus/version assessed, including the evidence cut-off date and a retrievable document register. Domain judgements must be reasoned from documented evidence; they are not converted into points or summed.

Programme and jurisdiction	[...]	Decision being assessed	[...]
Implementation stage	☐ Pre-pilot ☐ Pilot ☐ Scale-up ☐ Routine ☐ Modification	Assessment date	[...]
Matrix version	ELSI Readiness Matrix v1.0 (August 2026)	Evidence reviewed	[Evidence corpus/document register and evidence cut-off date]
Assessing body	[...]	Participants and declared interests	[...]

Permitted domain judgements: *Sufficient for this stage | Sufficient with conditions | Insufficient for this stage | Not applicable, with justification.*

Application principle. *Each domain should be considered in relation to the specific decision and implementation stage under assessment. Evidence should be documented and uncertainty made explicit. Domain judgements are not converted into points or combined into an aggregate score.*

1. Governance and decision-making architecture

Coded readiness items (Table 1)	Evidence and current status	Gap, condition or action required
D1.1 Programme mandate, legal authority and responsible decision-making bodies.	[Cite documents, data and stakeholder evidence]	[...]
D1.2 Transparent condition-selection criteria, procedures and public rationales.	[Cite documents, data and stakeholder evidence]	[...]
D1.3 Stakeholder and public participation, representation, expertise and conflicts of interest.	[Cite documents, data and stakeholder evidence]	[...]
D1.4 Accountability, review, appeal and programme change-control procedures.	[Cite documents, data and stakeholder evidence]	[State missing, contested or low-certainty evidence]
Domain judgement	☐ Sufficient for this stage ☐ Sufficient, with conditions ☐ Insufficient for this stage ☐ Not applicable	

Rationale / priority actions: [...]

2. Child-centred justification and proportionality

Coded readiness items (Table 1)	Evidence and current status	Gap, condition or action required
D2.1 Untreated phenotypic spectrum, severity, penetrance, expressivity and age at onset in screened populations.	<i>[Cite documents, data and stakeholder evidence]</i>	[...]
D2.2 Clinical validity, actionability, intervention effectiveness and burden.	<i>[Cite documents, data and stakeholder evidence]</i>	[...]
D2.3 Incremental child-centred benefit over existing screening and diagnostic pathways.	<i>[Cite documents, data and stakeholder evidence]</i>	[...]
D2.4 Proportionality assessment of uncertainty, false positives, overdiagnosis, psychosocial harms and opportunity costs, with non-child utilities reported separately.	<i>[Cite documents, data and stakeholder evidence]</i>	[...]
Domain judgement	☐ Sufficient for this stage ☐ Sufficient, with conditions ☐ Insufficient for this stage ☐ Not applicable	

Rationale / priority actions: [...]

3. Consent, information and communication

Coded readiness items (Table 1)	Evidence and current status	Gap, condition or action required
D3.1 Antenatal, accessible and evaluated information.	<i>[Cite documents, data and stakeholder evidence]</i>	[...]
D3.2 Publicly justified participation and consent model, including genuine refusal.	<i>[Cite documents, data and stakeholder evidence]</i>	[...]
D3.3 Distinct authorisation or legal bases, where applicable, for screening, research, retention and clinical reuse.	<i>[Cite documents, data and stakeholder evidence]</i>	[...]
D3.4 Communication and counselling for negative, positive, uncertain, carrier and familial findings, including age-appropriate disclosure and later assent or re-consent.	<i>[Cite documents, data and stakeholder evidence]</i>	[...]
Domain judgement	☐ Sufficient for this stage ☐ Sufficient, with conditions ☐ Insufficient for this stage ☐ Not applicable	

Rationale / priority actions: [...]

4. Genomic data, residual samples and privacy governance

Coded readiness items (Table 1)	Evidence and current status	Gap, condition or action required
D4.1 Retained specimens, data products, data flows and permitted purposes.	<i>[Cite documents, data and stakeholder evidence]</i>	[...]
D4.2 Legal bases, responsible stewardship, access, linkage and security.	<i>[Cite documents, data and stakeholder evidence]</i>	[...]
D4.3 Retention periods, secondary or commercial use, parent or child access, withdrawal, deletion or destruction.	<i>[Cite documents, data and stakeholder evidence]</i>	[...]
D4.4 Validation, reanalysis, clinical reuse, recontact, follow-up and the child's developing authority.	<i>[Cite documents, data and stakeholder evidence]</i>	[...]
Domain judgement	☐ Sufficient for this stage ☐ Sufficient, with conditions ☐ Insufficient for this stage ☐ Not applicable	

Rationale / priority actions: [...]

5. Structural equity

Coded readiness items (Table 1)	Evidence and current status	Gap, condition or action required
D5.1 Equitable access to information, the screening offer and informed participation.	<i>[Cite documents, data and stakeholder evidence]</i>	[...]
D5.2 Population and ancestry representation and equitable genomic interpretation.	<i>[Cite documents, data and stakeholder evidence]</i>	[...]
D5.3 Territorial, socioeconomic and cultural access to confirmation, treatment, surveillance and follow-up.	<i>[Cite documents, data and stakeholder evidence]</i>	[...]
D5.4 Subgroup outcomes, equity impact assessment, public trust, mitigation and monitoring.	<i>[Cite documents, data and stakeholder evidence]</i>	[...]
Domain judgement	☐ Sufficient for this stage ☐ Sufficient, with conditions ☐ Insufficient for this stage ☐ Not applicable	

Rationale / priority actions: [...]

6. Clinical, organisational and economic capacity

Coded readiness items (Table 1)	Evidence and current status	Gap, condition or action required
D6.1 Laboratory, bioinformatics and quality systems, including turnaround and QA/QI.	[Cite documents, data and stakeholder evidence]	[...]
D6.2 Workforce and referral, confirmation, counselling, treatment and surveillance pathways.	[Cite documents, data and stakeholder evidence]	[...]
D6.3 Recurrent financing, economic evaluation, opportunity costs and long-term sustainability.	[Cite documents, data and stakeholder evidence]	[...]
D6.4 Registries, outcome and harm monitoring, evaluation and predefined procedures to modify, pause or withdraw components.	[Cite documents, data and stakeholder evidence]	[...]
Domain judgement	☐ Sufficient for this stage ☐ Sufficient, with conditions ☐ Insufficient for this stage ☐ Not applicable	

Rationale / priority actions: [...]

Dissent record

Dissent ID	Item or domain	Alternative position and rationale	Supporting evidence	Participant(s) or role(s)	Resolution status and effect on judgement
DR-01	[...]	[...]	[...]	[...]	[Resolved / unresolved; explain effect]

Material disagreements should be recorded rather than resolved by forced consensus. Unresolved dissent should be reflected in the relevant domain judgement and, where relevant, in the overall conclusion.

Overall conclusion (select one):

- ☐ Proceed
- ☐ Proceed conditionally
- ☐ Defer

Reasoned justification	[Explain how evidence, domain judgements, gaps and conditions support the conclusion. Do not report or infer an aggregate score.]
Critical unmet obligation(s)	[Identify any issue that independently warrants deferral.]
Priority actions / conditions	[List the principal actions or safeguards required before progression or continued implementation.]
Responsible body / bodies	[...]
Next review	[Specify date or evidence trigger, required outputs and responsible body.]

Decision rule. A critical unmet obligation—for example, lack of timely confirmation or effective treatment—may justify deferral even when other domains are sufficiently developed.

Decision authorisation

Authorisation outcome	<i>[Validated / validated with conditions / returned for revision / not validated]</i>
Authorising body	<i>[...]</i>
Authorised representative(s) and role(s)	<i>[...]</i>
Signature or formal approval record	<i>[Signature, minutes reference, resolution identifier or equivalent]</i>
Authorisation date	<i>[...]</i>