RESEARCH INVENTION JOURNAL OF RESEARCH IN MEDICAL SCIENCES 5(1):110-121, 2026

©RIJRMS Publications

ONLINE ISSN: 1115- 6198

Print ISSN: 1597-3107

https://doi.org/10.59298/RIJRMS/2026/51110121

Newborn Screening Expansion Using Long-Read Sequencing: Benefits, Harms, and Public Health Decision Frameworks Methods, Challenges, and Future Directions

Bwanbale Geoffrey David

Faculty of Pharmacy Kampala International University Uganda

ABSTRACT

The integration of long-read sequencing (LRS) into newborn screening (NBS) programs offers transformative potential for public health by enhancing diagnostic yield, resolving complex genetic variants, and providing expanded carrier and prenatal information. Compared to traditional short-read sequencing, LRS improves resolution of structural variants, splice events, and repeat expansions, facilitating earlier and more precise interventions. However, the expansion introduces challenges, including data privacy concerns, ethical dilemmas, incidental findings, equity considerations, and workforce and infrastructure requirements. Public health decision frameworks that systematically evaluate benefits, harms, economic implications, and stakeholder perspectives are essential for guiding implementation. Pilot studies, phased rollouts, and comparative effectiveness and cost-effectiveness analyses provide critical evidence for real-world application. Future research should focus on technological validation, data stewardship, workforce capacity, and policy alignment to ensure equitable, safe, and effective adoption of LRS in NBS programs.

Keywords: Newborn Screening, Long-Read Sequencing, Genomic Variants, Public Health Decision Framework, and Ethical and Equity Considerations.

INTRODUCTION

The expansion of newborn screening (NBS) to include long-read genomic sequencing has the potential to improve diagnostic detection, enable differentiation between genetic conditions, and facilitate targeted clinical interventions [1]. Yet it could also generate ambiguous findings, pose ethical challenges, and provoke indecision between screening modalities. A public health screening decision analytical framework incorporating benefits, harms, and economic aspects affords a transparent means to analyze expansion with long-read sequencing, weighing policy implications against existing consideration of short-read technology [2]. Long-read, compared to short-read, genomic sequencing provides high-length and low-duplicate sequencing of intronic material, regardless of genomic repeat content, improved resolution of complex and structural variants, and richer information on splice and gene fusion variants; analysis approaches distinguish between carrier (genetic predisposition) and non-carrier status (no genetic predisposition)[3]. These aspects drive NBS implementation interest in public health policy and screening feasibility. Widespread NBS policy and consideration of continued benefit-diagnostic complexity balance guide subsequent analysis of long-read technology for expansion readiness, potential additional advantage of early determination of genomic variants, and systematic appraisal of associated evidence [4]. Newborn screening (NBS) identifies serious health conditions in infants during the first days of life, enabling early medical intervention that can help reduce morbidity, mortality, and other impacts. Early neonatal screening can avert many sequelae for conditions such as congenital hypothyroidism (CH) and phenylketonuria (PKU) by initiating therapy during the first week of life. Currently, NBS policy applies to classical conditions that present in early infancy, or to identifiable emerging variants of such conditions. The twenty-two core, consensus NBS conditions from the Standard for Newborn Screening in the United States consist of five groups: [1] end-organ disorders, [2] inborn errors of metabolism, [3] immunologic disorders, [4] hemoglobinopathies, and [5] endocrinologic disorders.

Genomic sequencing not only holds the potential to address many of these existing screening gaps but can also identify expanded conditions of interest. While candidate conditions may exceed eighty, only approximately eight, with the possible addition of a ninth, achieve regular continued screening after screening considerations and systematic evidence review of analytical and clinical aspects [2]. While policy decisions around sequencing approaches are being pursued, screening currently focuses on shorter-read technology. Long-read technology has emerged as a promising option that could also be considered, and sequencing decisions remain under deliberation [6].

Background on Newborn Screening and Long-Read Sequencing

Newborn screening (NBS) for phenylketonuria began in 1963, and Dunkelberg & Dyer (1965) noted the incorporation of similar programs within state health departments throughout the 1970s in the United States [1]. By 2022, many states offered expanded NBS panels, typically screening for >50 disorders, and large studies documented follow-up resources in place [1]. Over 80 disorders, including sickle cell disease, congenital hypothyroidism, and cystic fibrosis, were initially targeted based on the availability of effective treatments. The cumulative incidence at birth of NBS disorders, based on real-world data from the CDC evaluated between 2016 and 2020, was reported at 1 in 226, with clear distinctions across states [2]. In 2021, more than 10 million newborns were screened, and 1 in 3 UK newborns underwent a screening test for developmental dysplasia of the hip [1]. Traditional NBS approaches from dried blood spots (DBS) remain limited by: [1]patients having NBS disorders display biochemical or physiologic abnormalities detectable from DBS, and [2] the disease, a newborn screens positive for requiring treatment or clinical monitoring within early infancy. Long-read sequencing (LRS) targeted the NBS space as well [7]. Several FDA-approved NBS panels number >50, many covering >100 biochemical compounds, with particular priority given to genes within the PKU and/or NBS areas. Genomic sequencing aimed to characterize more disorders while positioning responsibility more favorably with clinicians familiar with rare disorders than with general metabolic conditions [2]. Newborn genome sequencing (NBSeq) was being actively pursued or implemented in state programs when the broader NBS interest also occurred [8].

Methodological Frameworks for Decision Making

Long-read sequencing, a technology using advanced sequencing techniques (e.g., PacBio, Oxford Nanopore, 10x Genomics) to produce much longer sequence reads than previously available, offers considerable benefits for newborn screening over existing short-read approaches [9]. Long-read sequencing holds the potential to transform the newborn screening paradigm, moving from the current focus on a limited set of target conditions and the use of short-read sequencing, to a broader, richer application in which the possibility of assessment for an expanded range of conditions (e.g. carrier status), more fully accessible genome representation, and the early-life availability of prenatal information as and if these data are provided contribute to a richer, still life-first, yet also second-generation, newborn screening application[10]. With long-read sequencing, the range of genomes amenable to single-test de novo analysis increases, and the proportion of specifications resolvable at first-screen remains higher than with short-read sequencing [11]. Evidence has been gathered from the research literature concerning the analytical validity, clinical validity, and clinical utility of long-read sequencing applied to newborn screening, and considered systematically according to a decision-analytic modelling approach. Implementing long-read sequencing within the newborn screening framework: [1] engages the considerable public-health concern for adoption and promotion of newborn screening; and [12] anticipates potential advances rather than simply solving existing problems.

Evidence Synthesis in Genomic Screening

Long-read sequencing offers direct and comprehensive analysis of triple-helical expansions and other complex mutations hidden from short-read assemblers, enabling straightforward classification of pathogenicity according to the ACMG/AMP framework [13]. Newborn-screening pathways emphasize the importance of Early Attended Interventions therapies, monitoring, or referral that take place during inpatient or outpatient follow-up appointments in the first month after birth [14]. Within the current short-read-policy context, sequencing takes place before discharge; subsequently, pathway-appropriate variants become diagnostic only when resolution is sufficient for sequencing or when downstream data becomes available, for example, extended carrier status when prenatal data have already informed planning [15].

Stakeholder Engagement and Ethical Considerations

Newborn screening programs are increasingly exploring the inclusion of genomic sequencing. Stakeholder engagement is essential to assess the advantages and disadvantages of integrating large-scale sequencing into newborn screening [4]. Various engagement models exist to facilitate informed discourse on such public-health issues. Ethical scrutiny throughout the process is crucial [16]. Genomic sequencing results present complex components that challenge the implementation of established consent frameworks for newborn screening. Therefore, stakeholder consultation is imperative to determine the necessity, feasibility, mode, and framework of public engagement prior to initiating sequencing-related discussions [17]. To enable long-read sequencing in newborn screening, readiness and capacity need to be evaluated across six criteria: analytical validity, clinical

utility, patient acceptability, equity, sustainability, and the adoption of corresponding thresholds 1. For countries where traditional newborn screening already operates, such assessments should identify whether a pilot study or full implementation can proceed [18]. Continuous monitoring of performance, population-level oversight, and periodic re-evaluation are also essential after inclusion [4]. Parallel processes of capacity and stakeholder readiness evaluations can facilitate informed deliberations on capacity while establishing a foundation for broader engagement [19].

Economic Evaluation and Resource Allocation

Economic evaluations and resource allocation models have traditionally focused on short-read sequencing approaches, but must also encompass long-read sequencing strategies. Various candidate conditions and data inputs for these methods have been defined [20]. Outcomes of interest include cost, budget impact, augmented resource needs, and cost-effectiveness analysis with associated budget-impact modelling; characterised decision-analytic models encompass a detailed description, design rationale, and implementation roadmap [1]. Budget frameworks may consider opportunity costs and the perspective of different payers. Assignment of budgets proceeds downward through levels corresponding to individuals, families, and communities, where the distinction between opportunity cost and budget remains paramount [21]. Limited existing formal economic evaluations estimate that, under specific assumptions, short-read sequencing retains favourable cost-effectiveness throughout [5].

Benefits of Long-Read Sequencing in Newborn Screening

Long-read sequencing (LRS) is defined as the objective of generating sequenced reads whose lengths significantly exceed the throughput of the sequencer used, typically with lengths of 10 kb or greater [22]. Long-read sequencing approaches can generate sequence data that includes useful biological context at the nucleotide level. In DNA sequencing, long-read technologies provide accessible and industrial-scale protocols for sequencing entire human genomes, with three hours of hands-on preparation time and 24 hours of run time. Generated sequence data facilitates Single-Molecule Real-Time Genomic sequencing of ample human-sized reference genomes; the sequencing of human exomes and targeted resequencing is also feasible [7]. Existing solutions can address up to 99.4% of human exons, efficiently amplify large genome segments through long-range PCR, and deliver GenBank sequence-ready human genome assembly and annotation. Single-Molecule Real-Time sequencing functions through four-component reversible terminator technology [23]. The analysis of supplemental permanent units provides additional information for assessing the presence or absence of unnatural DNA and protecting against 5-hydroxymethylcytosine deposits. Conclusively, polymerization has an effect on insert size, shifting beyond 8 kb and subsequently changing toward 3 kb, and the presence of multiple polymerization peaks, respectively. Efficient sequencing strategies are critical to improve coverage of the Y chromosome [1]. These steps underpin the prevailing trend toward long-read sequencing [1].

Diagnostic Yield and Variant Resolution

For genomics and newborn screening, the potential offered by long-read sequencing is considerable. Compared to short-read approaches, long-read sequencing generates reads that approach average human-genome size [3]. This facilitates the resolution of gauge structural variants, large insertions, deletions, duplications, and inversions that disrupt more than 50 base pairs and the unchallenged detection of metagenomic species [24]. From a newborn-screening perspective, long-read sequencing shifts the paradigm beyond the acute diagnostic phase to prolonged carrier screening [2]. Carriers of genetic diseases can be symptomatic at birth. They may subsequently utilize information obtained from decidual, cord-blood, or dried-blood-spot sampling to pepper their decision-making about behaviour or reproduction, for example [25]. Long-read sequencing exhibits a limited diagnostic default for a bundle of plausible explanations at birth. The diagnostic yield may reach 85% for those disorders with extended panel coverage, which arguably augments the remaining rate at infant screening without much prospect. Low-delivery variants miss detection in standard short-read workflows but receive functional annotation and variant prioritisation via long-read approaches [5]. Non-coding repeat expansions for myotonic dystrophy, fragile X tremor ataxia syndromes, and an isoform switch in Smith–Lemli–Opitz syndrome accordingly become resolvable [26].

Expanded Carrier and Prenatal Information

Expanded carrier status and prenatal information that long-read sequencing can provide after birth may aid in decision-making [5]. Knowledge of a prenatal condition or carrier state can inform choices around pregnancy management, prenatal testing, and reproductive options, including preimplantation genetic testing, gamete donation, and family planning [27]. For conditions with known prenatal phenotypes, the capacity to seek termination may be relevant when the carrier state is first detected. Affected individuals may require clinical reassessment if carrier status is learned later [5]. Counseling needs following the receipt of carrier or prenatal information may differ depending on whether first-line screening precedes testing [3]. The absence of expanded carrier or prenatal information remains a permissible option under the Young, Default, and Acceptable frame

comparison. In the absence of expanded carrier status or prenatal information, counseling may zero in on the few conditions associated with actionable clinical management [28].

Improved Time-to-Action and Clinical Outcomes

The interval between sample collection and clinical intervention constitutes a critical element for effective screening and timely treatment initiation [29]. Expanded newborn screening with long-read sequencing shapeshifts the screening paradigm, potentially addressing pre-symptomatic conditions and brackets disorders with transferable assessment and established treatment pathways [30]. Evidence of broadened carrier status alongside selection of early-onset disorders underscores complementary yet principally separate genomic insights. Although varied frameworks amenable to long-read sequencing and non-sequencing technologies facilitate strategic implementation, refinement of accompanying interventions remains foundational for optimal benefit [4]. Accordingly, models estimating diagnostic yield, result management, and monitoring are of value [5]. Measures subdividing screening effort, genome deployment, carrier information, genomic variant scrutiny, and laboratory cadence further elucidate the interplay between sequencing lapse and probable clinical translation [31].

Harms and Potential Risks

Expansion of newborn screening to include long-read sequencing may offer substantial benefits, yet several potential harms warrant consideration [2]. Long-read sequencing of newborns is likely to increase the size of genetic datasets relative to short-read sequencing; longer reads allow the detection of complex variants and phasing of alleles across contiguous genes, increasing resolution and potentially leading to pathogenicity reclassification [32]. Enhanced carrier-status information may further modify the interpretation of variants associated with late-onset diseases and inform reproductive choices [1]. Given the scale of newborn screening, expanded data-sharing requirements, and the potential for more extensive sharing of genomic and health data, elevated risks to data privacy could arise. Genetic data may increasingly be perceived as health data and carry additional public-health-related implications [33]. The number of screening assays performed may increase substantially, with the proportional rise likely larger than for datasets formed at later life stages. Expanded genomic data are especially vulnerable to cybersecurity attacks that compromise individual privacy [34]. Broader access to genomic data raises the risk of misuse for discriminatory purposes (e.g., life or disability insurance), and public trust may decline if vulnerable groups are perceived to bear disproportionate risks. Strategies such as data minimization, differential privacy, governance arrangements that limit sensitive access to certain groups, and approaches that avoid genomic sequence sharing can mitigate risks associated with genomic data linkage to accessed health information [2].

Privacy, Data Security, and Genetic Counseling Needs

Following expanded sequencing through newborn screening, understanding detailed genetic information increases privacy and security risks and generates a strong demand for genetic counseling [2]. Data are at risk of unwanted access by external parties, and sensitive information such as reproductive carrier status and predictive genomics information could be valuable to various actors [35]. The size of individual genomic sequencing files also increases the hazard of unauthorized access compared to traditional newborn screening. Several cybersecurity threats could damage infrastructure, hinder medical progression, or expose citizens to broader risk levels [1]. Governance structures are needed to enforce strong protocols for data deidentification, oversee data permissions, and provide oversight to platforms and actors handling genetic information [4]. During the review of individual consent models, parental decisions received emphasis, with a focus on regulating continued data retention beyond early childhood or at the time of reincorporation [36].

Incidental Findings and Psychological Impact

In the context of newborn screening with genome-wide sequencing, the potential for genomic incidental findings represents a significant policy consideration [3]. Genomic incidental findings are genetic variants that are detected in a child but are unrelated to the targeted diseases being screened, yet may still be important for the child or their family. For many available long-read variants, the likelihood of generating an incidental finding is low, although still non-zero; even when certain variants are excluded, incidental findings may arise from non-heritable variants [5]. The frequency of incidental or secondary findings can range from a few percent to nearly all individuals tested, depending on specific analytical methods and reporting practices. The option to return incidental findings is highly contentious and receives attention in diverse public health arenas [37]. The debate is especially pronounced between findings indicating conditions with highly effective interventions or preventive measures, and those associated with conditions that cannot be prevented or for which effective interventions are not available [38]. Amnesty models (where selected incidental findings are not returned) must also navigate the inherent ethical tensions underlying this question, including conflicts between obligations to respect future autonomy or ensure timely access to information, and the desire to provide adequate genetic privacy and social security against stigmatisation, discrimination, or economic disadvantages across various life stages [2].

Equity, Access, and Health Disparities

Expanding newborn screening with long-read sequencing may inadvertently exacerbate health disparities if access to testing is unequal or if the associated benefits and harms vary across groups. Screening uptake rates have been substantially lower among rural and underserved populations [39]. These groups may also receive different, frequently lower benefits from screening, further amplifying disparities [3]. Technology is not uniformly beneficial; where population-level implementation and equity frameworks are lacking, it might be better to defer expansion. Addressing equity gaps in current public health programs should be prioritized over considering new public health interventions [1]. Long-read sequencing may provide immense benefits to diverse population segments. Yet, large-scale population-level adoption of long-read sequencing may advance before information is available to adequately judge the equity consequences of expansion, analyze the available equity data, or refine screening strategies to preserve equity [40]. Long-read sequencing holds transformative potential for basic clinical care and research. Public health decision frameworks must incorporate equity considerations to optimize health impact [5].

Public Health Decision Frameworks

Long-read sequencing can substantially improve newborn screening by maximizing the value of genomic data and informing actionable interventions [2]. However, implementing long-read sequencing throughout this cascade warrants a careful assessment of benefits, harms, and accompanying public health decision frameworks [2]. Existing scholarship emphasizes a range of analytical-epidemiological, policy-ethical, economics-resource, and implementation-considerations both within and beyond the newborn screening domain [1]. These diverse methods around objectives aim to enhance the availability of timely and equitable newborn screening extensions. A systematic evaluation framed within the distinct but complementary lens of newborn screening constitutes a notable addition to extant approaches [5].

Criteria for Implementation

Newborn screening (NBS) programs identify children at risk of developing serious health conditions and enable early treatment that can prevent morbidity and mortality [3]. Traditionally, NBS programs measure analytes in blood collected from a heel prick and analyze dried blood spots. Dried blood spots are stable at room temperature, facilitating transport to central laboratories while preserving user anonymity. Several countries have considered or begun supplementing traditional NBS with genomic sequencing of dried blood spots [1]. Although several genome-scale sequencing technologies could be adapted for NBS use [41, 42], long-read sequencing (LRS) offers unique advantages that make it particularly suitable for this application [2]. Long-read sequencing resolves complex genomic regions that remain ambiguous with short-read technologies. For example, many disease-causing variants involve structural changes that are difficult to capture accurately with current short-read approaches. Although short-read sequencing detects ~9 out of 10 pathogenic variants reported in publicly available patient databases, LRS detects all of these variants and many additional pathogenic variants that effectors propose for incorporation into NBS programs. Modern LRS platforms generate high-quality genomic data from dried blood spots collected during routine heel-prick NBS within a time frame compatible with clinical workflows and can complete whole-genome sequencing in under 48 hours [43]. In principle, each newborn's sequenced data could remain in the possession of health authorities, allowing clinicians to query and receive pathogenic variant updates without requiring any administrative follow-up from parents [3]. Long-read sequencing can inform public health and clinical decisions that genotype and analyze reconstructed transcript metrics for up to two genes, monitor alternative splice events for two genes of interest, and identify pathogenic structural variants in 103 associated with use in NBS and mini-exon searching to resolve 201 add-event 2099 difficult-to-detect splicing ancillaries via external public health-requested variant confirmation [4]. When evaluated individually, each variant falls below C2, and the genomic detection framework remains below the established C2 threshold [2].

Governance, Oversight, and Regulatory Considerations

The governance and oversight of newborn screening programs incorporating long-read sequencing must acknowledge the complexity and multi-stakeholder character of public health policy [1]. Newborn screening programs have a long tradition of strict governance amid competing equity and efficiency arguments [3], but the addition of long-read sequencing at scale introduces additional questions concerning oversight bodies, regulatory mechanisms, and accountability [1]. Governance structures are relevant to frameworks for evidence-generation and decision-making. Oversight bodies determine how evidence is generated and interpreted; they may approve specific technologies or methods used; they can independently issue recommendations, endorse or refute other bodies' conclusions; and they can specify how implementation, including research agendas, aligns with public health principles [2]. Newborn screening governance thus involves the broader concept of program oversight and encompasses requisite regulatory considerations.

Monitoring, Evaluation, and Quality Assurance

Continuous monitoring and periodic evaluation are critical to identify whether framed newborn screening programs remain aligned with targeted public health objectives and warrant their sustained implementation [1]. Certain performance indicators should be tracked on an ongoing basis, while a comprehensive appraisal of the broader, long-term consequences accompanying system evolution should occur at regular intervals [2]. Provisions for rapid investigation of unanticipated developments should also be incorporated [3]. Within the information obtained through this continual examination, specified quality-assurance measures and complementary efforts to assure data integrity can foster ongoing program coherence with prevailing long-term objectives [44]. Procedures for periodic reassessment thus become neglected, linked with frameworks for the complete re-evaluation of all aspects of the program, accompanied by adjustment as appropriate [5]. Despite its evident importance, the monitoring, evaluation, and quality assurance of expanded newborn screening using long-read sequencing or any other technology are rarely emphasized in public health literature. In the absence of plans for their incorporation, efforts to realize implementation may similarly stagnate [3].

Methods for Real-World Evaluation

Long-read sequencing (LRS) has the potential to expand newborn screening programs by providing information about both rare congenital disorders detectable in blood-spot samples and carrier status for genetic conditions that may affect unaffected siblings later in life [1]. Additional data about carrier status and parental genotypes obtained at birth have important implications for early-life management and reproductive planning. A framework for the public health evaluation of long-read sequencing as an adjunct to newborn screening has been developed, encompassing two types of "decision frameworks" that organize evaluation objectives: [1] anticipated benefits and harms, including cost; and [2] pragmatic evaluation of real-world effectiveness and cost-effectiveness, together with the necessary methods for each. Several approaches are possible for the real-world evaluation of long-read sequencing in newborn screening programs, and each is described in turn: [1] pilot studies, which implement long-read sequencing on a limited scale and evaluate benefits and harms (including costs) through targeted data collection; [2] pragmatic studies, which assess effectiveness and cost-effectiveness by comparing real-world outcomes for long-read sequencing to outcomes in matched cohort studies in which only short-read sequencing is performed; and [3] longitudinal studies, which track multiple types of impact over time following long-read sequencing adoption, based on the premise that these different types may evolve at differing rates. Pilot programs seek to establish long-read sequencing as an effective tool for newborn screening under real-world conditions [7]. The term "pilot study" is used broadly to encompass a variety of design approaches, including phased rollouts that broaden coverage over time. A specific pilot design is proposed that consists of a statewide scale-up in implementation, with cohorts expanding from the state capital to outlying regions, permitting systematic observation of the intervention's public health effects [45]. Each newborn receives either long-read sequencing or standard short-read sequencing, depending on the assignment of the state by birth (i.e., statewide randomization). The design minimizes practical concerns, such as consent and the shareability of data between institutions. Long-read sequencing is augmented with datasets generated through standard approaches, without requiring extra samples to monitor long-term consequences [7]. Priorities for data capture include strands relevant for assessing initial benefits and harms, along with a subset focused on understanding more distal criteria [5]. Pragmatic studies compare the real-world performance of long-read sequencing against that of short-read sequencing in a manner that approximates a randomized control trial. Such studies are feasible given the large number of public health systems that have yet to adopt long-read sequencing. Study protocols have been established based on methods for assessing the comparative effectiveness of alternative vaccines, allowing evaluation alongside existing pilot programs or independent implementation [46]. Pivotal clinical problems include determination of sequencing yield (variants detected) and laboratory time (time to reporting) in relation to recipient outcomes, and a second focus also considers time between recipient birth and public health follow-up, since longer delays tend to allow more opportunity for detrimental outcomes to emerge[4]. Follow-up studies investigate the impacts of long-read sequencing when implemented over a sustained period. Relevant intermediary and ultimate outcomes span the spectrum of public health priorities [7].

Pilot Studies and phased Rollout

The implementation of newborn screening using long-read sequencing could proceed through a series of pilot studies followed by phased rollout if those studies establish sufficient safety, effectiveness, and value [5]. Pilot studies would address remaining feasibility, acceptability, and stakeholder engagement questions, while phased rollout would evaluate real-world effectiveness and effectiveness alongside ongoing collection of genetic data [6]. Pilot study designs could offer screening alongside currently available tests for a limited period before the collection of additional data extends the monitoring period [8]. The studies could introduce screening services, monitor acceptability and feasibility, capture data, assess population-level access, and inform strategizing of follow-on studies [6]. Newborn screening and follow-on short-read lessons could inform new approaches to monitoring recruitment, representing a major opportunity to improve long-read implementation efficacy and

population health. A pilot study like BabyScreen + is underway in Victoria, Australia, to investigate the feasibility of conducting genomic newborn screening, specifically long-read sequencing, during pregnancy or shortly after birth [6]. Where the collection of long-read sequencing data is impractical, an optional parallel BabySeq offer evaluates carrier status and identifies care coordination opportunities for a subset of participants with known prenatally reported variants [8]. Phased rollout would extend implementation to additional jurisdictions or facilities already screened by pilot studies and introduce long-read sequencing system-wide at sites, adding screening capability through new investment [6]. Pragmatic designs align closely with real-world operations, specify screening alongside country or jurisdiction-specific formats, and establish matched-cohort comparators [5]. These studies would characterize care-seeking behaviour following screening and the timing of clinical interventions, and assess implementation programme alignment with perceived public health and distribution of net benefits across societal segments. Studies monitoring full population cohorts could document budget impact over longer time periods before and after screening [8].

Comparative Effectiveness and Cost-Effectiveness Analyses

Comparative effectiveness and cost-effectiveness analyses can provide insights into the expected healthcare impacts of public health strategies, and thus inform policy decisions regarding the implementation of long-read sequencing in newborn screening [5]. Comparative effectiveness and cost-effectiveness models can be leveraged to evaluate the expected healthcare impacts of long-read sequencing incorporation in newborn screening [3]. These models can facilitate decision-making between public health stakeholders by establishing a systematic evaluation framework and defining relevant decision criteria while accommodating various data interpretations [2]. Relevant cost and budget-impact scenarios can be analyzed from both system and payer perspectives, considering investment thresholds that reflect government purchasing power and funding limitations [5]. In parallel, the existing state of long-read sequencing technology and projected technological advancements can be characterized, allowing for careful consideration of deployment feasibility and enabling diverse public health objectives to be addressed simultaneously [1,6].

Outcomes Measurement and Longitudinal Follow-Up

Longitudinal follow-up of individuals constitutes a core component of public health, yet measures for this type of follow-up currently remain elusive despite widespread recognition of its significance [7]. The necessity for longitudinal follow-up becomes paramount after newborn screening expansion through long-read sequencing, which enables more definitive diagnosis and offers various clinical options [1]. Accompanying concerns pertain to incomplete ascertainment of individuals, differential loss-to-follow-up between early and late information-needing conditions, and socioeconomically disadvantaged groups [8]. Longitudinal follow-up for specific indicators permits monitoring, insight generation, and predictive modeling for a range of conditions [8]. The choice of specific indicators for longitudinal observation, as well as the strategies and approaches for data capture, including mitigation of loss to follow-up, constitutes an important area for focus [7].

Practical, Ethical, and Legal Considerations

The historic precedent of newborn screening as a public health strategy offers lessons for emerging frameworks proposed for sequencing newborn genomes [8]. The challenges of expanding screening remain significant, but the continued exploration of newborn sequencing offers opportunities to collaborate and enhance the ethical landscape surrounding the generation of genomic data at birth [6]. Expanded screening exposes newborns to potential harms, including parental distress, uninformative maternal carrier information, and uncertainty regarding the evolution of data usage and future clinical actionability [5]. Responsive engagement of stakeholders, such as families, newborn screening programs, and public health authorities, enables timely learning, anticipatory stewardship, and system-wide reflection that increases societal benefit and collective understanding while safeguarding the interests of newborns and their families [4]. Considerations pertaining to consent, equity, data sharing, and governance, often thought of as adjuncts to scientific or technical challenges, represent core aspects of the newborn sequencing agenda that could inform a broader array of genetic initiatives intended to enhance population health and enable newborns to benefit more equitably from rapidly developing genomic discoveries [3].

Informed Consent in Newborn Contexts

Long-read sequencing (LRS) is an innovative genomic technology that allows for the efficient analysis of complex genomic regions critical to newborn screening [1]. When integrated into existing newborn screening programs, LRS provides an alternative to short-read sequencing technologies, enabling the identification of a wider range of genetic conditions earlier in life [5]. The basic sequencing principle involves the generation of extéremely long reads from real-time polymerase chain reaction (PCR) signal, improving de novo assembly of complex genomes and phasing of structure-variant haplotypes [7]. Long-read data prove especially useful for variant resolution in genomic regions containing highly homologous sequence repeats, such as the SMN and CFTR genes. Therefore, a major advantage of a newborn screening program incorporating LRS is the ability to detect and act upon pathogenic variants that would not be reported using an ultra-rapid short-read sequencing approach, ultimately

accelerating time-to-action for patients and providers[8]. Long-read data generated during these sequences, consisting of approximately 1 GB of raw data and aligned to a reference genome, further exceed standard short-read data volumes and can offer a comprehensive view of carrier status for numerous conditions of varying clinical relevance [7].

Data Stewardship and Reuse

Data stewardship comprises the policies, practices, and management needed to maximize the use of data in ways that are useful and ethically appropriate [7]. Data-sharing initiatives should prioritize demonstration projects that use whole genome sequencing (WGS) to expand NBS across the genomic spectrum of disorders. Providing data as a service to the medical and scientific communities can accelerate the implementation of genomic medicine at every stage of life [8]. Such data-sharing activities can facilitate the collection and reporting of the evidence required by health policy stakeholders and create stronger links between researcher and clinician communities [6]. Data stewardship principles should include agreements for data reuse, as well as standards to promote the de-identification of sequences and relevant genomic information [47]. Aesthetics encompass all the factors that influence the acceptability of the information conveyed to users of data gathered during NBS, including the clarity of the message and the way that sensitive details are handled [6]. Balancing yes-no schemes, colour-coding, bandwidth specifications, and data access options across many forms is essential to avoid elongating the delivery of time-sensitive truths [1].

International Collaboration and Harmonization

How newborn screening initiatives can benefit from international collaboration and harmonization [8]. Collaboration among countries and international organizations enables the sharing of resources, evidence, and lessons learned to strengthen efforts to expand newborn screening [5]. Internationally harmonized guidelines can reduce duplication of efforts, enhance the sharing of best practices, and encourage broader engagement of stakeholders and the public [1]. Cross-border data governance is critical for studies or pilots that require the sharing of sequencing and screening data from multiple countries or datasets with different privacy and ethical standards [6]. Collaboration to establish guidance on how to navigate legal requirements and obligations will facilitate multinational data governance [7].

Challenges and Barriers to Adoption

Expanding newborn screening with long-read sequencing (LRS) is expected to provide substantial benefits but faces challenges that merit thorough examination [1]. There are several barriers to implementation, including costs, policy, technology, and workforces that need to be addressed 2. Societal values, ethical principles, and public health frameworks should guide consideration of adoption [2].

Technological and Bioinformatic Hurdles

Long-read sequencing technology provides a unique opportunity to extend the scope of genomic analysis in newborn screening [1]. While short-read sequencing is already being used to complement traditional newborn screening for metabolic conditions, long-read methods support a much broader range of analyses [7]. Notably, long-read primary data offer the potential to resolve 95% of clinically relevant variants present at or near the single-cell level; address structural variation, repeat expansion, haplotype phasing, and mitochondrial analysis; enable simultaneous analysis of medically actionable germline and somatic variants; and allow the inclusion of additional data types such as transcriptome sequencing, proteomics, and methylation. Analysis pipelines can readily be adapted to address long reads, and bioinformatic prerequisites can be satisfied by widely available software 1 and scalable compute resources [5]. Implementation of long-read sequencing newborn screening is impeded by several technological and bioinformatic hurdles [3]. Data volumes, although smaller than for short reads, remain substantial (~200 gigabases per 24 hours per instrument) and demand ongoing development of acquisition, processing, and archiving workflows. Validation pipelines capable of verifying complex genome- and sample-specific analyses yet compatible with the rapid turnarounds required for newborn screening are still sought. Interoperability between long-read sequencing platforms and existing informatics frameworks further complicates integration into current genomics operations, especially in the absence of supplementary methods to convert primary data into universally supported intermediate formats [2].

Workforce and Infrastructure Requirements

The infrastructure for newborn screening (NBS) expansion with long-read sequencing (LRS) will require investments in workforce development, laboratory facilities, data storage capacity, and informatics systems [1]. The intervention is anticipated to follow a multiplexed, once-in-a-lifetime screening pathway that can operate independently from or in conjunction with other multiplex NBS tests, which currently utilize shortened genome-assembly approaches [3]. The number of samples requiring parallel long-read LRS processing per year at a given facility remains to be determined. Injector capacity and LRS throughput estimates from Oxford Nanopore flow cells and PacBio Sequel II SMRT Cells indicate that 64 to 256 newborn samples could be processed in a single flow-cell run [2]. Based on previously published estimates of 5,000 to 18,000 intermediate to severe cases eligible for NBS, with LRS adjusted to reflect the shorter time since introduction of multiplex NBS correlated with a rapid

increase in the total number of enrolled newborns, an intervention readily scalable to facilities with 64 to 256 sample injectors would accommodate the anticipated demand[4].

Policy and Reimbursement Barriers

Barriers related to policy, reimbursement, and payers complicate the introduction of long-read sequencing for newborn screening [8]. Traditional approaches often impose programmatic requirements that long-read sequencing may not satisfy. To smooth the transition to long-read sequencing, various policy and reimbursement mechanisms offer opportunities for phased implementation not contingent on meeting all barriers for conventional screening [7]. Prioritizing advocacy and policy action to introduce long-read sequencing would confer substantial public health benefits, while ongoing and operationalized short-read sequencing for carrier screening would foster incremental improvements and maintain equivalence with existing platforms [1]. The implementation of long-read sequencing for newborn screening faces several challenges pertaining to policy, reimbursement, and payers. Current policy frameworks place conditions on introducing new tests or technologies that long-read sequencing is unlikely to fulfil during its early adoption [5]. By establishing mechanisms that do not require meeting conventional newborn-screening program barriers, a phased approach would enable broader knowledge accumulation on the expected public health contributions of long-read sequencing. Selecting and fostering advocacy and policy options that permit long-read sequencing implementation would address significant decision-analytic question marks and potentially yield large population benefits, especially since the investment already underpins ongoing carrier-screening platform operations for prenatal samples [8].

Future Directions and Research Agendas

Expansion of newborn screening programs with long-read sequencing has the potential to generate substantial public health benefits, but implementation also entails meaningful risks [7]. A framework for analysing this opportunity considers the expected benefits and harms alongside a variety of public health decision frameworks. Individual components of the framework have been characterised based on existing literature and analysis. The anticipated direction of future work, together with associated research priorities, can therefore be aligned with remaining public health objectives [48-53]. Summarised below are key questions that can guide upcoming investigations [54-57]. What technologies and bioinformatics solutions enable the use of long-read sequencing in newborn screening? What is the current status of validation pipelines, interoperability standards, and the capacity to perform long-read sequencing on a scale relevant to population screening?[8] How do human resources, infrastructure, and training needs for long-read sequencing compare to those for existing screening technologies? What capacity is needed to support the anticipated scale of population screening? What reimbursement policies and payer perspectives compromise the adoption and implementation of long-read sequencing in newborn screening? What policy and advocacy measures can mitigate these barriers? [58-60].

CONCLUSION

Long-read sequencing represents a promising evolution in newborn screening, offering higher diagnostic accuracy, earlier identification of actionable genetic conditions, and expanded information for carrier and prenatal decision-making. Its implementation, however, must be carefully guided by public health decision frameworks that weigh clinical benefits against ethical, privacy, and equity concerns. Pilot programs, real-world evaluations, and phased rollouts are essential to establish feasibility, cost-effectiveness, and population-wide impact. Investment in workforce development, infrastructure, and governance frameworks will be critical to ensure the responsible and equitable integration of LRS into newborn screening. Strategic collaboration, continuous monitoring, and longitudinal follow-up will support evidence-based policy decisions and maximize societal benefit while mitigating potential harms.

REFERENCES

1. Shah N, Brlek P, Bulić L, Brenner E, Škaro V, Skelin A, Projić P, Shah P, Primorac D. Genomic sequencing for newborn screening: current perspectives and challenges. *Croatian Medical Journal.* 2024;65(3):261–267. doi:10.3325/cmj.2024.65.261.
2. Mitchell CO, Rivera-Cruz G, Chau MHK, Dong Z, Choy KW, Shen J, Amr S, Giersch ABS, Morton CC. The Burden and Benefits of Knowledge: Ethical Considerations Surrounding Population-Based Newborn Genome Screening for Hearing. *International Journal of Neonatal Screening.* 2022;8(2):36. doi:10.3390/ijns8020036.
3. Ugwu CN, Ugwu OP, Alum EU, Eze VH, Basajja M, Ugwu JN, Ogenyi FC, Ejemot-Nwadiaro RI, Okon MB, Egba SI, Uti DE. Sustainable development goals (SDGs) and resilient healthcare systems: Addressing medicine and public health challenges in conflict zones. Medicine. 2025 Feb 14;104(7):e41535.
4. Friedman JM, Cornel MC, Goldenberg AJ, Lister KJ, Sénécal K, Vears DF, et al. Genomic newborn screening: public health policy considerations and recommendations. *BMC Medical Genomics.* 2017;10:9. doi:10.1186/s12920-017-0247-4.
5. Jeanne M, Chung WK. DNA sequencing in newborn screening: opportunities, challenges, and future directions. Clinical Chemistry. 2025 Jan;71(1):77-86.

6. Kariyawasam DS, Scarfe J, Meagher C, Farrar MA, Bhattacharya K, Carter SM, Newson AJ, Otlowski M, Watson J, Millis N, Norris S. Integrating Ethics and Equity with Economics and Effectiveness for newborn screening in the genomic age: a qualitative study protocol of stakeholder perspectives. *PLOS ONE*. 2024. doi:10.1371/journal.pone.0299336.
7. Ugwu OP, Alum EU, Ugwu JN, Eze VH, Ugwu CN, Ogenyi FC, Okon MB. Harnessing technology for infectious disease response in conflict zones: Challenges, innovations, and policy implications. Medicine. 2024 Jul 12;103(28):e38834.
8. Oehler JB, Wright H, Stark Z, Mallett AJ, Schmitz U. The application of long-read sequencing in clinical settings. Human genomics. 2023 Aug 8;17(1):73.
9. Coventry PA, Pickstone JV. From what and why did genetics emerge as a medical specialism in the 1970s in the UK? A case-history of research, policy, and services in the Manchester region of the NHS. Social Science & Medicine. 1999 Nov 1;49(9):1227-38.
10. Lunke S, Bouffler SE, Downie L, Caruana J, Amor DJ, Archibald A, et al. Prospective cohort study of genomic newborn screening: BabyScreen+ pilot study protocol. *BMJ Open*. 2024;14(4):e081426.
11. Ongesa TN, Ugwu OP, Ugwu CN, Alum EU, Eze VH, Basajja M, Ugwu JN, Ogenyi FC, Okon MB, Ejemot-Nwadiaro RI. Optimizing emergency response systems in urban health crises: A project management approach to public health preparedness and response. Medicine. 2025 Jan 17;104(3):e41279.
12. Jansen ME, Lister KJ, van Kranen HJ, Cornel MC. Policy Making in Newborn Screening Needs a Structured and Transparent Approach. *Frontiers in Public Health*. 2017;5:53. doi:10.3389/fpubh.2017.00053.
13. Chung WK. The new newborn screening. Nature Medicine. 2025 Apr;31(4):1075-6.
14. Oehler JB, Wright H, Stark Z, Mallett AJ, Schmitz U. The application of long-read sequencing in clinical settings. Human genomics. 2023 Aug 8;17(1):73.
15. Hu T, Chitnis N, Monos D, Dinh A. Next-generation sequencing technologies: An overview. Human immunology. 2021 Nov 1;82(11):801-11.
16. Ermini L, Driguez P. The application of long-read sequencing to cancer. Cancers. 2024 Mar 25;16(7):1275.
17. Ugwu CN, Ugwu OP, Alum EU, Eze VH, Basajja M, Ugwu JN, Ogenyi FC, Ejemot-Nwadiaro RI, Okon MB, Egba SI, Uti DE. Medical preparedness for bioterrorism and chemical warfare: A public health integration review. Medicine. 2025 May 2;104(18):e42289.
18. Slovin S, Carissimo A, Panariello F, Grimaldi A, Bouché V, Gambardella G, Cacchiarelli D. Single-cell RNA sequencing analysis: a step-by-step overview. RNA bioinformatics. 2021 Apr 10:343-65.
19. Chen G, Ning B, Shi T. Single-cell RNA-seq technologies and related computational data analysis. Frontiers in genetics. 2019 Apr 5;10:317.
20. Friedman JM, Cornel MC, Goldenberg AJ, Lister KJ, Sénécal K, Vears DF. Genomic newborn screening: public health policy considerations and recommendations. BMC Medical Genomics. 2017 Feb 21;10(1):9.
21. Paul-Chima UO, Basajja M, Fabian CO, Chinyere NU, Ben OM, Mustafa MM. Neuro-entero-cardiac bridge: could gut-derived catecholamine-loaded extracellular vesicles synchronize the pathogenesis of Parkinson's disease, irritable bowel syndrome, and stress-triggered arrhythmias?. Medical Hypotheses. 2026 Feb 7:111896.
22. Zhang Z, Cui F, Lin C, Zhao L, Wang C, Zou Q. Critical downstream analysis steps for single-cell RNA sequencing data. Briefings in bioinformatics. 2021 Sep;22(5):bbab105.
23. Andrews TS, Kiselev VY, McCarthy D, Hemberg M. Tutorial: guidelines for the computational analysis of single-cell RNA sequencing data. Nature protocols. 2021 Jan;16(1):1-9.
24. Szakállas N, Barták BK, Valcz G, Nagy ZB, Takács I, Molnár B. Can long-read sequencing tackle the barriers, which the next-generation could not? A review. Pathology and Oncology Research. 2024 May 16;30:1611676.
25. Edyedu I, Ugwu OP, Ugwu CN, Alum EU, Eze VH, Basajja M, Ugwu JN, Ogenyi FC, Ejemot-Nwadiaro RI, Okon MB, Egba SI. The role of pharmacological interventions in managing urological complications during pregnancy and childbirth: A review. Medicine. 2025 Feb 14;104(7):e41381.
26. Oehler JB, Wright H, Stark Z, Mallett AJ, Schmitz U. The application of long-read sequencing in clinical settings. Human genomics. 2023 Aug 8;17(1):73.
27. Ermini L, Driguez P. The application of long-read sequencing to cancer. Cancers. 2024 Mar 25;16(7):1275.
28. Llewellyn S, Procter R, Harvey G, Maniatopoulos G, Boyd A. Facilitating technology adoption in the NHS: negotiating the organisational and policy context a qualitative study. Health and Social Care Delivery Research. 2014 Jul 30;2(23):1-32.

29. Ugwu OP, Ogenyi FC, Ugwu CN, Ugwu MN. Gut microbiota-derived metabolites as early biomarkers for childhood obesity: A policy commentary from urban African populations. Obesity Medicine. 2025 Sep 1;57:100641.
30. Ziegler A, Chung WK. Universal newborn screening using genome sequencing: early experience from the GUARDIAN study. Pediatric Research. 2025 Mar;97(4):1315-9.
31. Berg JS, Powell CM. Potential uses and inherent challenges of using genome-scale sequencing to augment current newborn screening. Cold Spring Harbor perspectives in medicine. 2015 Dec 1;5(12):a023150.
32. Berg JS, Powell CM. Potential uses and inherent challenges of using genome-scale sequencing to augment current newborn screening. Cold Spring Harbor perspectives in medicine. 2015 Dec 1;5(12):a023150.
33. Ugwu OP, Ogenyi FC, Ugwu CN, Basajja M, Okon MB. Mitochondrial stress bridge: Could muscle-derived extracellular vesicles be the missing link between sarcopenia, insulin resistance, and chemotherapy-induced cardiotoxicity?. Biomedicine & Pharmacotherapy. 2025 Dec 1;193:118814.
34. Woerner AC, Gallagher RC, Vockley J, Adhikari AN. The use of whole genome and exome sequencing for newborn screening: challenges and opportunities for population health. Frontiers in Pediatrics. 2021 Jul 19;9:663752.
35. Kingsmore SF. Newborn testing and screening by whole-genome sequencing. Genetics in Medicine. 2016 Mar 1;18(3):214-6.
36. Johnston J, Lantos JD, Goldenberg A, Chen F, Parens E, Koenig BA, NSIGHT Ethics and Policy Advisory Board. Sequencing newborns: a call for nuanced use of genomic technologies. Hastings Center Report. 2018 Jul;48:S2-6.
37. Howard HC, Knoppers BM, Cornel MC, Wright Clayton E, Sénécal K, Borry P. Whole-genome sequencing in newborn screening? A statement on the continued importance of targeted approaches in newborn screening programmes. European journal of human genetics. 2015 Dec;23(12):1593-600.
38. Guthrie R, Susi A. A simple phenylalanine method for detecting phenylketonuria in large populations of newborn infants. Pediatrics. 1963;32:338-343.
39. Roman TS, Crowley SB, Roche MI, Foreman AKM, O'Daniel JM, et al. Genomic Sequencing for Newborn Screening: Results of the NC NEXUS Project. Am J Hum Genet. 2020;107(4):596-611. doi:10.1016/j.ajhg.2020.08.001.
40. Adhikari AN, Gallagher RC, Wang Y, Currier RJ, Amatuni G, et al. The role of exome sequencing in newborn screening for inborn errors of metabolism. Nat Med. 2020;26(9):1392-1397. doi:10.1038/s41591-020-0966-5.
41. Kingsmore SF, Smith LD, Kunard CM, et al. A genome sequencing system for universal newborn screening, diagnosis, and precision medicine for severe genetic diseases. Am J Hum Genet. 2022;109(9):1605-1619. doi:10.1016/j.ajhg.2022.08.003.
42. Holm IA, Agrawal PB, Ceyhan-Birsoy O, Christensen KD, et al. The BabySeq project: implementing genomic sequencing in newborns. BMC Pediatr. 2018;18:225. doi:10.1186/s12887-018-1200-1.
43. Rosenbaum S. Data governance and stewardship: designing data stewardship entities and advancing data access. **Health Serv Res.** 2010;45(5 Pt 2):1442-1455. doi:10.1111/j.1475-6773.2010.01140.x.
44. Peng G, Privette JL, Tilmes C, Bristol S, Maycock T, Bates JJ, et al. The state of assessing data stewardship maturity—an overview. **Data Sci J.** 2018;17:7. doi:10.5334/dsj-2018-007.
45. National Research Council (US). **Ensuring the integrity, accessibility, and stewardship of research data in the digital age.** Washington (DC): National Academies Press; 2009.
46. Knoppers BM. Framework for responsible sharing of genomic and health-related data. **HUGO J.** 2014;8:3. doi:10.1186/s11568-014-0003-1.
47. Rehm HL, Page AJH, Smith L, Adams JB, Alterovitz G, Babb LJ, et al. GA4GH: International policies and standards for data sharing across genomic research and healthcare. **Cell Genom.** 2021;1(2):100029. doi:10.1016/j.xgen.2021.100029.
48. Lawson J, Cabili MN, Kerry G, Boughtwood T, Thorogood A, Alper P, et al. The Data Use Ontology to streamline responsible access to human biomedical datasets. **Cell Genom.** 2021;1(2):100028. doi:10.1016/j.xgen.2021.100028.
49. O'Doherty KC, Shabani M, Dove ES, Bentzen HB, Borry P, Burgess MM, et al. Toward better governance of human genomic data. Nat Genet. 2021;53(1):2-8. doi:10.1038/s41588-020-00742-6.
50. Friedman JM, Cornel MC, Goldenberg AJ, Lister KJ, Sénécal K, Vears DF, et al. Genomic newborn screening: public health policy considerations and recommendations. BMC Med Genomics. 2017;10(1):9. doi:10.1186/s12920-017-0247-4.

51. Jansen ME, Lister KJ, van Kranen HJ, Cornel MC. Policy making in newborn screening needs a structured and transparent approach. Front Public Health. 2017;5:53. doi:10.3389/fpubh.2017.00053.
52. Carli D, Quarello P, Porta F, et al. A genomic sequencing approach to newborn mass screening and its opportunities. JAMA Netw Open. 2025;8(10):e2538198. doi:10.1001/jamanetworkopen.2025.38198.
53. Morley KI, Leach B, Hocking L, Dawney J, Marciniak-Nuqui Z, Stockwell S, Yiangou D. Exploring the ethical dimensions of sequencing newborns' genomes: rapid literature and evidence review. Genomics England-commissioned report delivered by RAND Europe; Aug 2022.
54. Bick D, Ahmed A, Deen D, Ferlini A, Garnier N, Kasperaviciute D, et al. Newborn screening by genomic sequencing: opportunities and challenges. Int J Neonatal Screen. 2022;8(3):40. doi:10.3390/ijns8030040.
55. Cherniack M, Lahiri S. Barriers to implementation of workplace health interventions: an economic perspective. Journal of Occupational and Environmental Medicine. 2010 Sep 1;52(9):934-42.
56. Müller JM. Assessing the barriers to Industry 4.0 implementation from a workers' perspective. IFAC-PapersOnLine. 2019 Jan 1;52(13):2189-94.
57. Anwar F, Shamim A. Barriers in adoption of health information technology in developing societies. International journal of advanced computer science and Applications. 2011;2(8).
58. Kulkov I, Tsvetkova A, Ivanova-Gongne M. Identifying institutional barriers when implementing new technologies in the healthcare industry. European Journal of Innovation Management. 2023 Jun 8;26(4):909-32.
59. Weinstein M, Cheddie K. Adoption and implementation barriers for worksite health programs in the United States. International Journal of Environmental Research and Public Health. 2021 Nov 16;18(22):12030.
60. Tsai R, Alterman T, Grosch JW, Luckhaupt SE. Availability of and participation in workplace health promotion programs by sociodemographic, occupation, and work organization characteristics in US workers. American Journal of Health Promotion. 2019 Sep;33(7):1028-38.

CITE AS: Bwanbale Geoffrey David (2026). Newborn Screening Expansion Using Long-Read Sequencing: Benefits, Harms, and Public Health Decision Frameworks Methods, Challenges, and Future Directions. RESEARCH INVENTION JOURNAL OF RESEARCH IN MEDICAL SCIENCES 5(1):110-121. https://doi.org/10.59298/RIJRMS/2026/51110121