



Implications of Newborn Screening for Nurses

Jane DeLuca, PhD, RN, CPNP, APNG¹, Karen L. Zanni, MSN, ARNP-BC, RN-C², Natasha Bonhomme, BA³, & Alex R. Kemper, MD, MPH, MS⁴

1 Epsilon Xi, Associate Professor of Clinical Nursing, University of Rochester School of Nursing, Rochester, NY, USA

2 Delta Phi, Nursing Doctoral Student, Binghamton University, Decker School of Nursing, Binghamton, NY, USA

3 Vice President of Strategic Development, The Genetic Alliance, Washington, DC, USA

4 Associate Professor of Pediatrics, Duke University School of Medicine, Durham, NC, USA

Key words

Neonatal screening, ethics, genome, nursing practice

Correspondence

Dr. Jane M. DeLuca, University of Rochester School of Nursing, 601 Elmwood Ave Box 50N, Rochester, NY 14611, USA.

E-mail: Jane_deluca@urmc.rochester.edu

Accepted: October 28, 2012

doi: 10.1111/jnu.12005

Abstract

Purpose: Newborn screening has dramatically decreased the morbidity and mortality associated with a wide range of heritable conditions. Continuing advances in screening technology and improvements in the effectiveness of treatment are driving the rapid expansion of newborn screening programs. In this article, we review issues in newborn screening care and opportunities for nurses and nursing faculty to provide education and conduct research to improve the impact of newborn screening.

Organizing Construct: This article provides (a) an overview of current newborn screening activities, including how conditions are added to newborn screening panels and how implementation occurs at state and national levels; (b) a description of current controversies and ethical considerations; (c) a description of the roles of nurses in the newborn screening process; (d) suggestions for nursing education and research; and (e) a summary of expected future developments in newborn screening, including genome sequencing.

Conclusions: Nurses are uniquely well suited to address the educational needs and future research in newborn screening because of the role that nurses play in the provision of direct clinical care and in population-based healthcare delivery.

Clinical Relevance: Newborn screening is a public health approach to the identification of rare but treatable conditions in early infancy. In the United States, as in other industrialized countries, newborn screening is rapidly expanding. Nurses, nurse educators, and nurse researchers are positioned to contribute to the field of newborn screening by assuring programs are implemented safely and effectively, by facilitating education of the nursing work force, and by developing and contributing to research programs in newborn screening.

The goal of newborn screening is the early identification and treatment of conditions associated with significant morbidity or mortality (Moyer, Calonge, Teutsch, & Botkin, 2008). Newborn screening began in the 1960s through analysis of dried-blood spots for a single disorder, phenylketonuria. The development of new screening technology and therapeutic interventions beginning in the 1980s has led to rapid expansion of newborn screening. Newborn screening has dramatically decreased the morbidity and mortality for infants with rare, heritable conditions and congenital disorders (Dijk, McKay, Barzi,

Gaskin, & Fitzgerald, 2011; Wilcken, 2012). However, increased growth and complexity of newborn screening programs and the emergence of advanced technologies in screening have raised critical issues related to ethics, care delivery, and research (Avard, Vallance, Greenberg, & Potter, 2007).

Diverse national and state policies govern newborn screening practices and the determination of conditions suitable for screening. In the United States, newborn screening programs operate at the state level. Because of this, variations have developed in the conditions

included in screening. To help guide states and to decrease this variability, a federal advisory committee, the U.S. Secretary of Health and Human Services Advisory Committee on Heritable Disorders in Newborns and Children (SACHDNC), was formed to provide guidance to the Secretary regarding which conditions should be included in newborn screening and how other aspects of screening, such as follow-up, should be coordinated (Howell & Lloyd-Puryear, 2010; Perrin et al., 2010). The recommended uniform newborn screening panel consists of those conditions recommended by the Secretary to states for screening. Funding for screening programs comes from Maternal and Child Health Services Title V block grants, state revenue, public health appropriations, and fees from families or insurance companies (Therrell et al., 2007).

In many European countries, newborn screening programs are coordinated and administered at the national level, with professional oversight conducted, in some instances, by national screening societies (Javaher et al., 2010). There is a call for a uniform panel of disorders across Europe similar to that in the United States (Loeber et al., 2012). Screening program and procedure costs are often covered by national or state agencies or in some cases by private insurers (Javaher et al., 2010). In Canada there is no national governance of newborn screening programs. Each province develops and administers screening programs for each region (Avard et al., 2007; Little et al., 2009).

In developing countries in the Asian Pacific, Latin America, and Middle East there is considerable interest in newborn screening, but implementing and sustaining newborn screening is difficult when there is potential political instability, poverty, and competing public health systems and priorities (Giugliani, 2010; Padilla, Krotoski, & Therrell, 2010). Screening efforts have been supported through sharing of expertise and resources from established programs in Europe (Padilla et al., 2010). Half the world's births occur in Asian Pacific countries; therefore, modest screening programs for a single disorder, such as hypothyroid screening in Laos, provide substantial benefits for children in these nations (Padilla & Therrell, 2012).

Balancing the Benefits and Harms of Newborn Screening

In general, conditions are recommended for newborn screening if there is sufficient evidence that early diagnosis leads to improved health outcomes and that the benefits of screening outweigh potential harms (Calonge et al., 2010). When developing recommendations for

new disorders for screening, the U.K. National Screening Committee and the SACHDNC examine evidence from systematic reviews and take into account factors such as economic feasibility, availability of treatment, and acceptability by the public of the screening test (U.K. National Screening Committee, 2012; Watson et al., 2006). Two conditions were recently added to the universal newborn screening panel in the United States: severe combined immunodeficiency disorder and congenital heart disease (Buckley, 2012; Kemper et al., 2011). Other conditions, including hemoglobin H disease, Krabbe disease, Pompe disease, and chronic bilirubin encephalopathy, have been considered but not recommended for screening (U.S. Department of Health and Human Services, 2012). The reasoning behind not adding these conditions was a lack of evidence for demonstrable benefits from early intervention, uncertainty about the feasibility of screening, and harms related to screening and diagnosis. Screening can identify secondary conditions, which are conditions not targeted by screening but detected in the process of screening. Deciding how screening programs should manage the detection of secondary conditions is challenging because these conditions may not be associated with serious disease and treatment strategies may not be established (Wilcken, 2010). For example, short-chain acyl-CoA dehydrogenase deficiency is detected in screening for metabolic disorders through tandem mass spectroscopy; however, the degree to which this condition is pathological is unclear (Wolfe, Jethva, Oglesbee, & Vockley, 2011).

In the United States, individual states can opt to screen for conditions not recommended by the SACHDNC. For example, screening for Krabbe disease, a progressive neurodegenerative disorder, began in New York State in 2006 prior to the SACHDNC recommendation not to include the disorder and continues today. There is limited evidence that supports long-term health benefits for infants treated with stem cell transplantation for infantile-onset Krabbe disease (Kemper et al., 2010). Pompe disease is a glycogen storage disorder with features of hypertrophic cardiomyopathy and weakened skeletal muscles. Enzyme replacement therapy has been used for a number of years, but it is expensive, and clinical improvements in cardiac arrhythmias and gross motor function are variable (Prater et al., 2012). The SACHDNC has not yet recommended newborn screening for Pompe disease, but Missouri, Illinois, and New Mexico have passed legislation for eventual screening of these disorders (Burton, 2012). When there is limited evidence of benefit from screening, there are decided tensions between the application of new technologies and protecting the public from potential harms of screening. On the other hand, opportunities for expanding knowledge and for refining

screening technologies and treatments are possible through population-based screening in the newborn period.

In developing newborn screening policy, the major focus has been on improving outcomes for affected newborns, but families may also benefit even when no specific treatment is available. Although early identification of some conditions (e.g., muscular dystrophy, fragile X syndrome) may not lead directly to decreases in morbidity or mortality in the affected child, such information could help the family avoid the challenge of seeking help from multiple healthcare providers before the diagnosis is established (the “diagnostic odyssey”), allow the family to make informed reproductive choices, and help the family prepare for the expected health outcome of the child (Bailey et al., 2009). Another argument regarding the benefit of early diagnosis of conditions for which early intervention may not improve health outcomes is that early identification may lead to the development of novel therapies (Bailey et al., 2009; Wilcken, 2011). Studies indicate that public support is high for early screening of untreatable conditions (Etchegary et al., 2012; Hasegawa, Fergus, Ojeda, & Au, 2011). Nevertheless, early diagnosis of “untreatable” conditions may lead to harm for families. In *The Changing Moral Focus of Newborn Screening* (President’s Council on Bioethics, 2008) authors cited negative effects of early screening for Duchenne muscular dystrophy, including disrupted parent-infant bonding, stress, anxiety, and parents seeking potentially hazardous treatments for their children.

Harms of Newborn Screening

The harms of screening are often difficult to quantify. It is important to recognize that screening tests are associated with both false-negative and false-positive test results. A false-negative result occurs when screening fails to identify a true diagnosis for an infant. Screening test specificity can reduce false-negative results, but as a consequence, more false-positive findings may be detected. The increase in the number of screening tests has increased the risk for false-positive results (Tarini, Christakis, & Welch, 2006). False positives, cases where presumed positive diagnoses are ruled out, can create substantial anxiety and stress for families at least until the work-up is completed (Schmidt et al., 2012). Effective communication between providers and parents can help reduce anxiety associated with any abnormal screening results (Davis et al., 2006).

More challenging, perhaps, are ambiguous or intermediate results identified in metabolic screening, for example, acylcarnitines for fatty acid oxidation disorders,

which may not normalize with repeat blood and urine biochemical testing. Uncertain results prompt a cascade of testing and ongoing monitoring until a diagnosis is confirmed or infants remain healthy and can be discharged from care. The effects of diagnostic uncertainties and prolonged engagement with health services for families have only begun to be explored. In a study of infants with uncertain metabolic diagnoses, some parents had ongoing worries about potential illness despite providers’ reassurances of normal health and growth for their infants (Timmermans & Buchbinder, 2010).

Screening for some conditions (e.g., sickle cell disease, cystic fibrosis) can lead to the identification of infants who are carriers of one abnormal allele. Most infants who are carriers have no direct medical problems but are at increased risk for having an affected child in the future. There is limited research on how carrier status can be discussed with parents in ways that allow them to make meaningful use of it (Lang, McColley, Lester, & Ross, 2011). Moreover, few studies have been undertaken that examined how children are informed about their carrier status by parents and providers (Ulph, Leong, Glazebrook, & Townsend, 2010).

Newborn screening requires only a fraction of the collected dried-blood spot for analysis. The remainder, known as the residual dried-blood spot, can be stored in biobanks and used for program quality assurance, validation of new assays, and epidemiological research (e.g., the population prevalence of specific genes or gene variants; Therrell et al., 2011). Residual dried-blood spots have been used for forensic purposes (e.g., identification of a missing newborn) and analyzed in cases of unexpected deaths (Norgaard-Pedersen & Hougaard, 2007). Biobanks are a rapidly developing strategy for not only storing dried-blood spots, but of balancing privacy protections when dried-blood spots are used for quality assurance and research. The storage and use of dried residual blood spots without parents’ permissions has sparked debates and legal action in the United States, the United Kingdom, and Australia (Lewis et al., 2011; Bowman & Studdert, 2011). Studies of parents’ responses to biobanking and use of dried-blood samples in research indicate parents will often participate in research when informed consent is obtained and privacy protections are in place (Bombard et al., 2012; Tarini et al., 2010). U.S. policies for parental permission for storage, destruction of samples, or use in research vary, but it can be expected that added focus on the disposition of blood spot samples will spur policy development (Haga, 2010). To promote greater understanding of biobanking among the public and for providers, education related to residual dried-blood spots use is needed (Botkin et al., 2012).

Newborn Screening in Nursing Practice, Education, and Research

Nurses and midwives are key providers for educating and communicating screening information to parents throughout the newborn screening process. Appropriately timed preemptive high-quality education may lessen distress associated with subsequent abnormal screening results and facilitate follow-up (Tluczek, Orland, Nick, & Brown, 2009).

Preconception Period

Educating expectant parents is challenging because of the large number and complexity of conditions and the limited amount of time that parents have to learn about newborn screening. Parents prefer that information and education about newborn screening be provided to them over the course of pregnancy and before delivery (Detmar et al., 2007; Hasegawa et al., 2011). Parent teaching and educational brochures should include descriptions of how screening results will be communicated back to families and what parents can expect if retesting or an evaluation is needed for their infants (Arnold et al., 2006; Davis et al., 2006).

Perinatal Period

Information about newborn screening is often presented to parents at some point after delivery, but in the excitement of a new baby this information may be lost. Globally, policies vary in requiring informed consent from parents for newborn screening. In the United States, newborn screening is considered a mandatory process with only a few states requiring formal consent procedures for screening (Therrell, Johnson, & Williams, 2006). Newborn screening usually operates with children being screened as a default. There are provisions in many states for parents to opt out of screening for religious and other reasons (Ross, 2010), but it is unclear how this information is presented to parents and how often they opt out of the process. Parents who refuse screening in the United States and elsewhere typically sign a form that outlines the potential health risks for the infant. In much of Europe, Australia, and New Zealand, newborn screening is voluntary, and written or verbal consent from parents is required (Human Genetics Society of Australia, 2011; Kerruish, Webster, & Dickson, 2008; Loeber et al., 2012). In a qualitative study by Nicholls (2012), Canadian parents stated they had minimal discussions about consent, with screening performed as a routine part of postnatal care. This suggests possible shortcomings in obtaining fully informed consent in clinical

settings. In screening for conditions for which the benefit is uncertain, screening should ideally be conducted within a research protocol, including informed consent and prospective evaluation of the impact of screening on newborns and families (Kemper & Wake, 2007; Ross & Waggoner, 2012).

The cornerstone of newborn screening has been the analysis of dried-blood spots in centralized public health laboratories, which has the benefits of providing a mechanism for public health programs to assure that all newborns are screened and to allow public health officials to monitor follow-up. Two conditions, congenital hearing loss and critical congenital heart disease, are based on physiological tests and can be screened for in the newborn nursery prior to discharge. In the future, it is likely that tests carried out in centralized laboratories could be performed within the newborn nursery. For example, "laboratory on a chip" screening devices would allow the rapid diagnosis of conditions that now rely on complex screening technology in public health laboratories (Millington et al., 2010). This approach allows for earlier diagnosis but would remove centralized public health laboratories from the process of screening.

Pediatricians and nurses are often first to inform families about abnormal newborn screening results, usually by telephone or a home visit. It is not uncommon for providers to have insufficient understanding of screening and lack confidence in speaking with parents about screening results (Dunn, Gordon, Sein & Ross, 2012; Kemper, Uren, Moseley, & Clark, 2006). Parents are often very distressed by the notification of an abnormal screen. Accessing the Internet for disease information can frighten parents and increase their distress (DeLuca, Kearney, Norton, & Arnold, 2012). Providers can help by guiding parents to credible newborn screening websites and engaging them in discussions of online information.

National or state boundaries can be barriers to practice if screening policies are markedly different in adjacent regions. Pediatric providers in the United States who care for patients across state borders should be familiar with policies governing screening practices for neighboring states (Newborn Screening Authoring Committee, 2008). Cross-border cooperation is encouraged among E.U. countries for sharing protocols, expertise, research, treatment, and follow-up (European Union Tender, 2012).

Specialty Care

Specialty care providers are central to the diagnosis and care of newborn screening patients. Multidisciplinary teams of geneticists, nutritionists, genetic counselors, and nurses are commonly employed because of the

complexity of the conditions. Extended wait times for metabolic clinic appointments, or sweat tests for cystic fibrosis, and waiting for results from diagnostic testing can be agonizing for families (DeLuca, Kearney, Norton, & Arnold, 2011; Tluczek, Kosciak, Farrell, & Rock, 2005). Nurses play an important role in the coordination and communications between primary or specialty care centers and parents for decreasing families' distress and managing children after diagnosis for improving health outcomes.

Long-Term Follow-Up

Historically, newborn screening programs have focused on assuring that newborns are appropriately screened and that those children with an abnormal screening result are either rescreened or have diagnostic follow-up (i.e., short-term follow-up). The benefit of newborn screening, however, comes from the long-term treatment of those identified with a condition. The SACHDNC has defined the components of long-term follow-up as high-quality chronic disease management with condition-specific treatment and age-appropriate preventive care over the lifespan (Hinton et al., 2011; Kemper et al., 2008). In recent years, state-based and voluntary national registries have developed in the United States for tracking and research of rare diseases. Gaps in long-term follow-up include shortages of specialists and lack of public awareness of the benefits of screening (Centers for Disease Control and Prevention, 2012). European screening systems provide expert short-term care, but long-term follow-up is organized locally without centralized long-term monitoring of patients (Burgard et al., 2012). Long-term follow-up is crucial for understanding the natural history of rare disorders and innovating and improving treatment. Raising public awareness through advocacy and the development of regulatory guidelines for follow-up may help close the gap in long-term service provision. Continuous quality assurance projects can help to identify areas for improvement in services to keep pace with rapid changes in newborn screening (Burgard et al., 2012; Hinton et al., 2011).

Opportunities for Nurse Educators

Nurse educators can prepare nursing students at different stages of their careers for clinical, research, and education roles related to families and newborn screening. For nursing faculty, newborn screening provides an elucidatory model for teaching clinical genetics. Metabolic disorders are largely autosomal recessive and rare; however, several disorders such as phenylketonuria have been extensively studied. Screening disorders can be used

for teaching students patterns of inheritance, metabolic pathways, and principles of metabolic diet therapy. Two websites, *GeneReviews* and *Online Mendelian Inheritance in Man* (see Clinical Resources), offer comprehensive information about screening disorders with links to primary references. Knowledge of tandem mass spectroscopy, DNA, and biochemical diagnostic testing can enrich the study of genetics and newborn screening for nurse faculty and trainees.

Clinically relevant newborn screening information can be explored through links to public health. Websites for state newborn screening departments of health and governmental agencies are substantive resources for policy information on screening practices (see Clinical Resources). The U.S. National Newborn Screening & Genetics Resource Center is an extensive website for information about state and international screening programs. Similarly, the U.K. Programme Centre and Orphanet are storehouses for information about disorders and service provision. Web resources such as the Newborn Screening Translational Network are freely available and can be used in class assignments and newborn screening topic discussions.

In addition, nursing faculty has used simulation with students in applying genomic knowledge in case studies (Daack-Hirsch, Dieter, & Quinn, 2011). Simulations for practice conversations can help students develop their communication skills and confidence in discussing newborn screening information or other complex genetic or educational information.

Nursing Research in Newborn Screening

There are a wide range of opportunities for nursing research in policy, ethics, and clinical research in newborn screening. Cost-effectiveness research is needed for weighing the relative costs and benefits of newborn screening. Further research of biobanking and use of screening samples are important areas of inquiry. Potential areas for investigation include examining disparities in newborn screening care as steps toward identifying system deficits and creating equitable screening systems. A compelling area of research is investigating the responses of the public toward newer screening technologies, such as whole genome analysis. Additional research is needed for understanding best practices in communication between providers and newborn screening parents. Nurse researchers are involved in the study of disease-specific biomarkers and molecular analyses. Examining epigenetic influences on diseases can further objectives of improving outcomes and health promotion for those affected by rare disorders. Furthermore, multidisciplinary

research and clinical teams are needed for the delivery of innovations from the bench to bedside and back.

Conclusions

Rapid advances in technology (e.g., DNA microarrays, digital microfluidics) will continue to expand the number of conditions that can be detected through newborn screening (Millington et al., 2010). Although prohibitively expensive now, the time may come when the entire genome could be sequenced as part of newborn screening. Recent debates highlight the challenges of applying newer technologies in screening common disorders and sequencing for personalized medicine (Goldenberg & Sharp, 2012). This raises concerns about how information from genome sequencing will be used by families for managing predisposition for adult-onset conditions. Managing more information generated by genome-wide screening may, at least at first, strain primary providers' abilities to effectively communicate information to parents (Tarini & Goldenberg, 2012). Public education will be critical for enhancing people's understanding of newer screening methods and for maintaining public trust.

As newborn screening technologies and systems continue to advance, the roles of nurses will also need to evolve to meet the new challenges for newborn screening practice. Nurse educators, researchers, and clinicians are needed for the translation of new scientific findings into practice and can lead the way for advancing genomic science in the service of patients and families.

Clinical Resources

- Baby's First Test: <http://www.babysfirsttest.org/>
- GeneReviews: <http://www.ncbi.nlm.nih.gov/gtr/>
- Genetic Alliance: <http://www.geneticalliance.org/>
- Genetic Home Reference: <http://ghr.nlm.nih.gov/>
- International Society for Newborn Screening: <http://www.isns-neoscreening.org/htm/home.htm>
- Orphanet: <http://www.orpha.net/consor/cgi-bin/index.php?lng=EN>
- National Coordinating for Genetics and Newborn Screening: <http://www.nccrg.org/>
- National Newborn Screening & Genetics Resource Center: <http://genes-r-us.uthscsa.edu/>
- Newborn Screening Translational Network: <https://www.nbstrn.org/>
- Online Mendelian Inheritance in Man (OMIM): <http://www.ncbi.nlm.nih.gov/gtr/>

- Save Babies Through Screening Foundation: <http://www.savebabies.org/>
- Secretary's Advisory Committee on Heritable Disorders in Newborns and Children: <http://www.hrsa.gov/advisorycommittees/mchbadvisory/heritabledisorders/>
- U.K. Newborn Screening Programme Centre: <http://newbornspot.screening.nhs.uk>

References

- Arnold, C. L., Davis, T. C., Frempong, J. O., Humiston, S. G., Bocchini, A., Kennen, E. M., & Lloyd-Puryear, M. (2006). Assessment of newborn screening parent education materials. *Pediatrics*, 117(5 Pt 2), S320–S325. doi:10.1542/peds.2005-2633L
- Avard, D., Vallance, H., Greenberg, C., & Potter, B. (2007). Newborn screening by tandem mass spectrometry: Ethical and social issues. *Canadian Journal of Public Health*, 98(4), 284–286.
- Bailey, D. B., Armstrong, F. D., Kemper, A. R., Skinner, D., & Warren, S. F. (2009). Supporting family adaptation to pre-symptomatic and “untreatable” conditions in an era of expanded newborn screening. *Journal of Pediatric Psychology*, 34(6), 648–661.
- Bombard, Y., Miller, F. A., Hayeems, R. Z., Carroll, J. C., Avard, D., Wilson, B.,... Charkraborty, P. (2012). Citizens' values regarding research with stored samples from newborn screening in Canada. *Pediatrics*, 129(2), 239–247. doi:10.1542/peds.2011-2572
- Botkin, J. R., Rothwell, E., Anderson, R., Stark, L., Goldenberg, A., Lewis, M.,... Wong, B. (2012). Public attitudes regarding the use of residual newborn screening specimens for research. *Pediatrics*, 129, 231–238. doi:10.1542/peds.2011-0970
- Bowman, D. M., & Studdert, D. M. (2011). Newborn screening cards: A legal quagmire. *Medical Journal of Australia*, 194(6), 139–322.
- Buckley, R. H. (2012). The long quest for neonatal screening for severe combined immunodeficiency. *Journal of Allergy and Clinical Immunology*, 129(3), 597–604.
- Burgard, P., Rupp, K., Linder, M., Haege, G., Rigter, T., Weinreich, S. S.,... Hoffmann, G. F. (2012). Newborn screening programmes in Europe; Part 2– From screening laboratory results to treatment, follow-up and quality assurance. *Journal of Inherited Metabolic Disease*, 35, 613–625. doi: 10.1007/s10545-012-9484-z
- Burton, B. (2012). Newborn screening for Pompe disease. *American Journal of Medical Genetics. Part C, Seminars in Medical Genetics*, 160(1), 8–12. doi:10.1002/ajmg.c.31315
- Calonge, N., Green, N. S., Rinaldo, P., Lloyd-Puryear, M., Dougherty, D., Boyle, C.,... Howell, R. R. (2010). Committee report: Method for evaluating conditions

- nominated for population-based screening of newborns and children. *Genetics in Medicine*, 12, 153–159. doi:10.1097/GIM.0b013e3181d2af04
- Centers for Disease Control and Prevention. (2012, June 1). CDC grand rounds: Newborn screening and improved outcomes. *Morbidity and Mortality Weekly Report*, 61(21), 390–393.
- Daack-Hirsch, S., Dieter, C., & Quinn, M. T. (2011). Integrating genomics in undergraduate nursing education. *Journal of Nursing Scholarship*, 43, 223–230. doi:10.1111/j.1547-5069.2011.01400.x
- Davis, T. C., Humiston, S. G., Arnold, C. L., Bocchini, J. A., Bass, P. F., Kennen, E. M.,... Lloyd-Puryear, M. (2006). Recommendations for effective newborn screening communication: Results of focus groups with parents, providers, and experts. *Pediatrics*, 117(5 Pt 2), S326–S340. doi:10.1542/peds.2005-2633M
- DeLuca, J. M., Kearney, M. H., Norton, S. A., & Arnold, G. L. (2011). Parents' experiences of expanded newborn screening evaluations. *Pediatrics*, 128(1), 53–61. doi:10.1542/peds.2010-3413
- DeLuca, J. M., Kearney, M. H., Norton, S. A., & Arnold, G. L. (2012). Internet use by parents of infants with positive newborn screens. *Journal of Inherited Metabolic Disease*, 35, 879–884. doi:10.1007/s10545-011-9449-7
- Detmar, S., Hosli, E., Dijkstra, N., Nijssingh, N., Rijnders, M., & Verweij, M. (2007). Information and informed consent for neonatal screening: opinions and preferences of parents. *Birth*, 34(3), 238–244. doi:10.1111/j.1523-536x.2007.00176.x
- Dijk, F. N., McKay, K., Barzi, F., Gaskin, K. J., & Fitzgerald, D. A. (2011). Improved survival in cystic fibrosis patients diagnosed by newborn screening compared to a historical cohort from the same centre. *Archives of Diseases in Children*, 96(12), 1118–1123. doi:10.1136/archdischild-2011-300449
- Dunn, L., Gordon, K., Sein, J., & Ross, K. (2012). Universal newborn screening, knowledge, attitudes and satisfaction. *Southern Medical Association*, 105(4), 218–222. doi:10.1097/smj.0b013e31824f8220
- Etchegary, H., Dicks, E., Hodgkinson, K., Pullman, D., Green, J., & Parfey, P. (2012). Public attitudes about genetic testing in the newborn period. *Journal of Obstetric, Gynecologic, & Neonatal Nursing*, 41(2), 191–200. doi:10.1111/j.1552-6909.2012.01341.x
- European Union Tender. (2012). *Evaluation of population newborn screening practices for rare disorders in member states of the European Union*. Retrieved from http://ec.europa.eu/eahc/documents/news/Report_NBS_Current_Practices_20120108_FINAL.pdf
- Giugliani, R. (2010). Inborn errors of metabolism in Latin American: Challenges and opportunities. *Journal of Inherited Metabolic Diseases*, 33(Suppl. 2), S315–S320. doi:10.1007/s10545-010-9112-8
- Goldenberg, A. J. & Sharp, R. R. (2012). The ethical hazards and programmatic challenges of genomic newborn screening. *Journal of the American Medical Association*, 307(5), 461–462. doi:10.001/jama.2012.68
- Haga, S. B. (2010). Analysis of educational materials and destruction/opt-out initiatives for storage and use of residual newborn screening samples. *Genetic Testing and Molecular Markers*, 14(5), 587–592. doi:10.1089/gtmb.2010.0010
- Hasegawa, L. E., Fergus, K. A., Ojeda, N., & Au, S. M. (2011). Parental attitudes toward ethical and social issues surrounding the expansion of newborn screening using new technologies. *Public Health Genomics*, 14(4–5), 298–306. doi:10.1159/000214644
- Hinton, C. F., Feuchtbaum L., Kus, C. A., Kemper, A. R., Berry S. A., Levy-Fisch, J.,... Boyle, C. A. (2011). What questions should newborn screening long-term follow-up be able to answer? A statement of the United States Secretary for Health and Human Services Advisory Committee on Heritable Disorders in Newborns and Children. *Genetics in Medicine*, 13(10), 861–865. doi:10.1097/GIM.0b013e3182209f09
- Howell, R. R., & Lloyd-Puryear, M. A. (2010). From developing guidelines to implementing legislation: Actions of the U.S. Advisory Committee on Heritable Disorders in Newborns and Children toward advancing and improving newborn screening. *Seminars in Perinatology*, 34(2), 121–124. doi:10.1053/j.semperi.2009.12.004
- Human Genetics Society of Australia. (2011). *Newborn bloodspot testing*. Retrieved from <https://www.hgsa.org.au/website/wp-content/uploads/2011/08/2011P02-Newborn-Bloodspot-Screening1.pdf>
- Javaher, P., Nyongui, E., Kaariainen, H., Kristofferson, U., Nippert, I., Sequeiros, J., & Schmidtke, J. (2010). Genetic screening in Europe. *Public Health Genomics*, 13(7–8), 524–537. doi:10.1159/000294998
- Kemper, A. R., Boyle, C. A., Aceves, J., Dougherty, D., Figge, J., Fisch, J. L.,... Howell, R. R. (2008). Long-term follow-up after diagnosis resulting from newborn screening: Statement of the U.S. Secretary of Health and Human Services' Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children. *Genetics in Medicine*, 10, 259–261. doi:10.1097/GIM.0b013e31816b64f9
- Kemper, A. R., Knapp, A. A., Green, N. S., Comeau, A., Metterville, D. R., & Perrin, J. M. (2010). Weighting the evidence for newborn screening for early-infantile Krabbe disease. *Genetics in Medicine*, 12(9), 539–543. doi:10.1097/GIM.0b013e3181e85721
- Kemper, A. R., Mahle, W. T., Martin, G. R., Cooley, W. C., Kumar, P., Morrow, W. R.,... Howell, R. R. (2011). Strategies for implementing screening for critical congenital heart disease. *Pediatrics*, 128, e1259–e1267. doi:10.1542/peds.2011-1317
- Kemper, A. R., Uren, R. L., Moseley, K. L., & Clark, S. J. (2006). Primary care physicians' attitudes regarding follow-up care for children with positive newborn

- screening results. *Pediatrics*, 118(5), 1836–1841. doi:10.1542/peds.2006-1639
- Kemper, A. R., & Wake, M. A. (2007). Duchenne muscular dystrophy: Issues in expanding newborn screening. *Current Opinion in Pediatrics*, 19(6), 700–704.
- Kerruish, N. J., Webster, D., & Dickson, N. (2008). Information and consent for newborn screening practices and attitudes of service providers. *Journal of Medical Ethics*, 34, 648–652. doi:10.1136/jme.2007.023374
- Lang, C. W., McColley, S. A., Lester, L. A., & Ross, L. F. (2011). Parental understanding of newborn screening for cystic fibrosis after a negative sweat test. *Pediatrics*, 127(2), 276–283. doi:10.1542/peds.2010-2284
- Lewis, M. H., Goldenberg, A., Anderson, R., Rothwell, E., & Botkin, J. (2011). State laws regarding the retention and use of residual newborn screening blood samples. *Pediatrics*, 127(4), 703–712. doi:10.1542/peds.2010-1468
- Little, J., Potter, B., Allanson, J., Caulfield, T., Carroll, J. C., & Wilson, B. (2009). Canada: Public health genomics. *Public Health Genomics*, 12, 112–120. doi:10.1159/000156113
- Loeber, J. G., Burgard, P., Cornel, M. C., Rigter, T., Weinreich, S. S., Rupp, K.,... Vittozzi, L. (2012). Newborn screening programmes in Europe; Part 1– From blood spot to screening result. *Journal of Inherited Metabolic Disease*, 35(4), 603–661. doi:10.1007/s10545-012-9483-0
- Millington, D. S., Ramakrishna, S., Eckardt, A., Rouse, J., Balie, D., Goldberg, R.,... Pamula, V. (2010). Digital microfluidics: A future technology in newborn screening laboratory? *Seminars in Perinatology*, 34(2), 163–169. doi:10.1053/j.semperi.2009.12.008
- Moyer, V. A., Calonge, N., Teutsch, S. M., & Botkin, J. R. (2008). Expanding newborn screening: Process, policy, and priorities. *Hastings Center Report*, 38(3), 32–39.
- Newborn Screening Authoring Committee, American Academy of Pediatrics. (2008). Newborn screening expands: Recommendations for pediatricians and medical homes– Implications for the system. *Pediatrics*, 121(1), 192–217. doi:10.15242/peds.2007-3021
- Nicholls, S. G. (2012). Proceduralisation, choice and parental reflections on decisions to accept newborn bloodspot screening. *Journal of Medical Ethics*, 38(5), 299–303. doi:10.1136/medethics-2011-100040
- Norgaard-Pedersen, B., & Hougaard, D. M. (2007). Storage policies and use of the Danish Newborn Screening Biobank. *Journal of Inherited Metabolic Diseases*, 30(4), 530–536. doi:10.1007/s10545-007-0631-x
- Padilla, C. D., Krotoski, D., & Therrell, B. L. (2010). Newborn screening process in developing countries-overcoming internal barriers. *Seminars in Perinatology*, 34, 145–155. doi:10.1053/j.semperi.2009.12.007
- Padilla, C. D., & Therrell, B. L. (2012). On consolidating newborn screening efforts in the Asia Pacific Region. *Journal of Community Genetics*, 3, 35–45. doi:10.1007/s12687-011-0076-7
- Perrin, J. M., Knapp, A. A., Browning, M. F., Comeau, A. M., Green, N. S., Lipstein, E. A.,... Kemper, A. R. (2010). An evidence development process for newborn screening. *Genetics in Medicine*, 12(3), 131–134. doi:10.1097/GIM.0b013e3181d28eb1
- Prater, S. N., Banugaria, S. G., DeArme, S. M., Botha, E. G., Stege, E. M., Case, L. E.,... Krishnani, P. S. (2012). The emerging phenotype of long-term survivors of infantile Pompe disease. *Genetics in Medicine*, 14, 800–816. doi:10.1038/gim.2012.44
- President's Council on Bioethics. (2008). *The changing moral focus of newborn screening: An ethical analysis by the President's Council on Bioethics*. Washington, DC: Author. Retrieved from <http://bioethics.georgetown.edu/pcbe/reports/newbornscreening/index.html>
- Ross, L. F. (2010). Mandatory vs. voluntary consent for newborn screening. *Kennedy Institute of Ethics Journal*, 20(4), 299–328. doi:10.1353/ken.2010.0010
- Ross, L. F., & Waggoner, D. J. (2012). Parents: Critical stakeholders in newborn screening. *Journal of Pediatrics*, 161(3), 385–389. doi:10.1016/j.peds.2012.04035
- Schmidt, J. L., Castellanos-Brown, K., Childress, S., Bonhomme, N., Oktay, J. S., Terry, S. F.,... Green, C. (2012). The impact of false-positive newborn screening results on families: A qualitative study. *Genetics in Medicine*, 14(1), 76–80. doi:10.1038/gim.2011.5
- Tarini, B. A., Christakis, D. A., & Welch, H. G. (2006). State newborn screening in the tandem mass spectrometry era: More tests, more false positive results. *Pediatrics*, 118(2), 448–456. doi:10.1542/peds.2005-2026
- Tarini, B. A., & Goldenberg, A. J. (2012). Ethical issues in newborn screening in the genomic era. *Annual Reviews Genomics and Human Genetics*, 13, 1–13. doi:10.1146/annurev-genom-090711-163741
- Tarini, B. A., Goldenberg, A. J., Singer, D., Clark, S. J., Butchart, A., & Davis, M. M. (2010). Not without my permission: Parents' willingness to permit use of newborn screening samples for research. *Public Health Genomics*, 13(3), 125–130. doi:10.1159/000228724
- Therrell, B. L., Hannon, W. H., Bailey, D. B., Goldman, E. B., Monaco, J., Norgaard-Pedersen, ... Howell, R. R. (2011). Considerations and recommendations for national guidance regarding the retention and use of residual dried blood spot specimens after newborn screening. *Genetics in Medicine*, 13(7), 621–624. doi:10.1097/GIM.0b013e3182147639
- Therrell, B. L., Johnson, A., & Williams, D. (2006). Status of newborn screening programs in the United States. *Pediatrics*, 117(Suppl. 3), S212–S252. doi:10.1542/peds.2005-2633C
- Therrell, B. L., Williams, D., Johnson, K., Lloyd-Puryear, M. A., Mann, M. Y., & Ramos, L. R. (2007). Financing newborn screening: sources, issues, and future considerations. *Journal of Public Health Management Practice*, 13(2), 207–213.

- Timmermans, S., & Buchbinder, M. (2010). Parents-in-waiting: Living between sickness and health in the genomics era. *Journal of Health and Social Behavior*, 51(4), 408–423. doi:10.1177/0022146510386794
- Tluczek, A., Kosciak, R. L., Farrell, P. M., & Rock, M. J. (2005). Psychosocial risk associated with newborn screening for cystic fibrosis: Parents' experience while awaiting the sweat-test appointment. *Pediatrics*, 115(6), 1692–1703. doi:10.1542/peds.2004-2075
- Tluczek, A., Orland, K. M., Nick, S. W., & Brown, R. L. (2009). Newborn screening: An appeal for improved parent education. *Journal of Perinatal and Neonatal Nursing*, 23(4), 326–334.
- U.K. National Screening Commission. (2012). *UK screening portal*. Retrieved from <http://www.screening.nhs.uk/policyreview>
- Ulph, F., Leong, J., Glazebrook, C., & Townsend, E. (2010). A qualitative study exploring genetic counselors' experiences of counseling children. *European Journal of Human Genetics*, 18, 1090–1094. doi:10.1038/ejg.2010.86
- U.S. Department of Health and Human Services, Secretary's Advisory Committee of Heritable Disorders in Newborns and Children. (2012). *Nominate a condition*. Retrieved from <http://www.hrsa.gov/advisorycommittees/mchbadvisory/heritabledisorders/nominatecondition/workgroup.html>
- Watson, M. S., Mann, M. Y., Lloyd-Puryear, M. A., Rinaldo, P., Howell, R. R. (2006). Newborn screening: Toward a uniform screening panel and system. *Pediatrics*, 117(5 Pt 2), S296–S307. doi:10.1542/peds.2005-26331
- Wilcken, B. (2010). Expanded newborn screening: reducing harm, assessing benefit. *Journal of Inherited Metabolic Diseases*, 33(Suppl. 2), S205–S210. doi:10.1007/s10545-010-9106-6
- Wilcken, B. (2011). Newborn screening: How are we travelling, and where should we be going? *Journal of Inherited Metabolic Disease*, 34(3), 569–574. doi:10.1007/s10545-011-9326-4
- Wilcken, B. (2012). Screening for disease in the newborn: The evidence base for blood-spot screening. *Pathology*, 44(2), 73–79. doi:10.1097/PAT.0b013e32834e843f
- Wolfe, L., Jethva, R., Oglesbee, D., & Vockley, J. (2011). Short-chain acyl-CoA dehydrogenase deficiency. *GeneReviews*. Retrieved from <http://www.ncbi.nlm.nih.gov/books/NBK63582/>