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Policy brief: Improve coverage of newborn genetic screening to include the Recommended Uniform Screening Panel and newborn screening registry

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Executive Summary

A major goal of newborn screening is to reduce morbidity and mortality in infants and children by identifying heritable conditions in which early treatment may improve a child's long-term health and survival. However, the number and type of heritable disorders included in newborn screening currently vary from state to state. Expert recommendations to screen for 34 core conditions and report on 26 secondary conditions were issued by the U.S. Department of Health and Human Services. This panel, known as the Recommended Uniform Screening Panel (RUSP), has not been adopted by all states thereby creating a geographic disparity in opportunities to receive timely intervention for potentially life-threatening heritable conditions. The Academy supports the recommendation to adopt the RUSP in newborn screening programs across all states and calls for the creation of a national newborn screening registry to improve monitoring of all affected infants. Further, the Academy recommends the extension of reporting and tracking to the 59 actionable variants when whole-genome sequencing is performed and supports the expansion of reporting as new actionable variants are detected.

Background

A major goal of newborn screening is to identify heritable conditions in which early intervention may improve a child's long-term health or survival (Solomon et al., 2012). The *Screening for Heritable Disorders* federal legislation was passed in 2000, and implemented in 2004, to enhance the ability of state and local agencies to provide screening and counseling, as well as health care services for newborns with actual or potential risk for

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heritable disorders (National Institute of Child Health and Human Development, n.d.). During that time, the Discretionary Advisory Committee on Heritable Disorders in Newborns and Children (DACHDNC, formerly known as the Secretary's Advisory Committee on Heritable Disorders in Newborns and Children) was chartered to provide recommendations to the Secretary of the U.S. Department of Health and Human Services regarding conditions to include in universal newborn screening and identify technologies, policies, and standards to reduce morbidity and mortality of newborns who have, or are at risk for, heritable disorders (Advisory Committee on Heritable Disorders in Newborns and Children, Health Resources and Services Administration of the United States Department of Health and Human Services, 2009). The DACHDNC considers many factors when making recommendations on which tests to add into newborn screening programs including whether (a) there is an accurate and reliable test for the disease, (b) the child's life would be improved by early detection and intervention, and (c) diagnosis and treatment are cost-effective. In addition to these criteria, the DACHDNC considers clinically significant conditions to include definitive identification of carrier status (U.S. Department of Health and Human Services, Advisory Committee on Heritable Disorders in Newborns and Children, 2016). In 2008, the *Newborn Screening Saves Lives Act* (H.R. 3825, S. 1858) was passed by Congress to add grant programs for education, follow-up care coordination, and new technology for newborn screening, to improve laboratory quality standards, and further define the role of the DACHDNC (Advisory Committee on Heritable Disorders in Newborns and Children, Health Resources and Services Administration of the United States Department of Health and Human Services, 2009; National Institute of Child Health and Human Development, n.d.; Solomon et al., 2012).

In 2009, the DACHDNC and Secretary of Health and Human Services recommended all state newborn screening programs to adopt the RUSP, a 30 core condition panel with 26 secondary conditions (RUSP, 2016). Since that time, 4 additional core conditions have been added to make the RUSP a 34 core condition panel with 26 secondary conditions. Secondary conditions of the RUSP can be identified through the screening process of the core conditions and can cause significant morbidity and/or mortality if they are not detected early in life (Solomon et al., 2012). The DACHDNC routinely considers the evidence related to adding screening tests to the RUSP. Recommendations from the DACHDNC are sent to the Secretary of Health and Human Services to consider, and a final recommendation is provided by the Secretary to state public health departments.

Core and secondary conditions are assessed via tandem mass spectrometry (MS/MS) using the newborn dried blood spot (NDBS) (Taylor, Wright, Hickey, & Housman, 2017). Although potentially 50 treatable inborn errors of metabolism can be detected through MS/MS, most states only test for a subset of these conditions due to cost and low frequency of selected conditions in some regions. Genetic abnormalities that are associated with major alterations of biochemicals in the blood can be detected. Other treatable conditions, including sickle cell disease, congenital hypothyroidism, cystic fibrosis, and severe combined immunodeficiency, are screened in the blood spot using other kinds of tests, such as high-performance liquid chromatography of hemoglobin or chemiluminescence. Two additional screening tests (congenital hearing loss and critical congenital heart disease) require physical measurements rather than blood testing.

When positive results are detected using MS/MS, which typically includes retesting and second-tier testing for confirmation, DNA-based testing can be used to confirm a positive result on the same blood spot used for the initial testing. DNA-based testing can be done by polymerase chain reaction, sequencing individual genes, sequencing using gene panels (a group of genes), or whole-genome or exome sequencing. Currently, targeted sequencing is only used as a secondary method in newborn screening programs to confirm positive test results for genetic disorders such as cystic fibrosis or sickle cell disease.

A major consideration when sequencing large gene panels or genome wide is the frequent occurrence of “incidental findings” otherwise referred to as “secondary findings.” These terms refer to when genetic variants of potential importance to the health of the child are identified but are unrelated to the disease for which testing is being performed. In 2013, the American College of Medical Genetics and Genomics (ACMG) published a recommended minimum list of 56 actionable genetic variants to be reported as incidental or secondary findings when performing clinical genomic sequencing to promote a system of standardized reporting (Green et al., 2013). A recent study found that more than 1% of the population carry pathogenic mutations in these genes and are at increased risk for common diseases regardless of whether the diseases are part of their family history (Natarajan et al., 2016). In 2016, the ACMG expanded this list of secondary findings to 59 actionable variants (Kalia et al., 2017).

Outside of research protocols, whole-genome sequencing is not yet used by newborn screening programs. Whole-genome sequencing has been shown, however, to improve the positive predictive value of prenatal genetic screening (Strom, Maxwell, & Owen, 2017) and may have similar applicability to newborn screening (Berg et al., 2013; Bodian et al., 2016). Inclusion of genome-wide sequencing performed as a component of newborn screening, or as part of the secondary testing procedures to confirm diagnosis, may be indicated. The use of whole-genome sequencing for confirmation of primary screening is reasonable when performed as part of a comprehensive program that includes genetic counselling, secure storage, public and professional education, and long-term follow up of genomic data, as new findings increase interpretability of results (Friedman et al., 2017; King & Smith, 2016). When whole-genome sequencing is used, the reporting of the currently identified 59 actionable variants is recommended, with the exception of parents who opt out of having the results returned to them (American College of Medical Genetics and Genomics, 2014). Additional actionable variants may be incorporated into this list in the future.

Nurses play a key role in newborn screening. They provide education and support to families as part of the care team and can help parents to understand the importance of detecting pathogenic variants that may predispose their child to a severe but preventable outcome (Taylor et al., 2017). Advanced practice nurses, especially nurse practitioners and certified nurse midwives, are care providers who assist in ensuring that screening is complete and that follow-up occurs. In addition, all nurses can work with legislators to advocate for RUSP recommendation adoption (Seibert, 2011).

Policy Options

Clear Disclosure of State RUSP Implementation Is Needed to Help Guide Parental Decision Making on Newborn Screening

The DACHDNC was created to provide expert recommendations to the U.S. Department of Health and Human Services regarding the conditions for which newborn screening programs would be responsible for detecting and development of policies and standards to reduce morbidity and mortality of newborns who have, or are at risk for, heritable disorders. The U.S. Department of Health and the Human Services and Health Resources and Services Administration have published recommendations for state implementation of newborn screening programs. However, because these agencies do not have the authority to implement a national newborn screening program, there is wide variation in the number of heritable conditions that are included in newborn screening at the state level.

Decisions regarding the number and types of heritable conditions to include in the newborn screening panel are currently made by each state's public health department, which is given authority to implement or refuse adoption of recommendations published by the Secretary of Health and Human Services (Advisory Committee on Heritable Disorders in Newborns and Children, Health Resources and Services Administration of the United States Department of Health and Human Services, 2009). At present, North Carolina screens for 29 conditions of the RUSP although the state newborn screening program screens for 37 conditions (Baby's First Test, 2017). Across the nation, all other states screen for 30 or more conditions of the RUSP. Similar to North Carolina, several states screen for a high number of conditions, although they do not include all recommended conditions of the RUSP (Taylor et al., 2017). Providing information to parents on whether the state is or is not following national recommendations for newborn screening and offering reasonable alternatives to add-on the tests included in the RUSP would provide an equitable solution.

Variability in Newborn Screening Procedures Across Each State Limits Equal and Optimal Screening for Newborns in Our Nation

Despite support of the RUSP recommendations by the DACHDNC, the Secretary of Health and Human Services, March of Dimes, and the American Academy of Pediatrics (AAP), many states base screening decisions on lack of funding or low incidence in their region (March of Dimes, 2017). However, there is evidence that the cost of completing the RUSP can save health care dollars and prevent undue suffering brought about by inability to quickly identify and manage or treat heritable disorders (Green et al., 2013). For instance, the state of California, which screens for over 40 conditions, saves $9.32 in health care cost for every dollar spent on newborn screening and exceeds annual program costs by $47.1 million (Feuchtbaum & Cunningham, 2006). Further, with racial/ethnic population admixture, prevalent internal migration of Americans across state lines, and the rapidly decreasing costs of genetic testing, the impact of implementing a universal newborn screening panel is more relevant today than in 2009 when originally proposed (Taylor et al., 2017).

Improved Monitoring and Follow-Up of Newborns and Children With Heritable Disorders Is Needed to Optimize Health Promotion and Prevention of Related Complications

Clinical professional organizations, such as the AAP, have raised concerns about timely screening as well as monitoring and follow-up of newborns with heritable disorders (American Academy of Pediatrics Newborn Screening Authoring Committee, 2008). In 2012, the DACHDNC provided recommendations to the Secretary of Health and Human Services supporting a process that would attach an NDBS serial number to each birth certificate in the electronic birth registration system (EBRS) in order to ensure timely, high-quality screening (American Academy of Pediatrics Newborn Screening Authoring Committee, 2008). At the time, the Secretary of Health and Human Services deferred this recommendation for future consideration because proposals to add a data element to the EBRS are only considered every 10 years. In addition, there were unresolved questions about the security, privacy and confidentiality of personal identifiable information, and concern over state autonomy for NBSP implementation. The opportunity to add a field for the NDBS to the U.S. Standard Certificate of Live Birth will reopen in 2019, and this provides the impetus for timely modification of the existing birth certificate template.

In addition, national organizations including the National Health Statistics and Information System, National Center for Health Statistics, and AAP, as well as DACHDNC, have recognized the need for national and/or regional back-up systems and redundancy to ensure continuity in newborn screening operations, including tracking (U.S. Department of Health and Human Services, 2012). As individuals and families often migrate across state lines, it is important to ensure continuity of care for individuals with heritable disorders. Recommendations for the development of a national electronic registry of newborn screening results will aid in follow up and care of screened infants (Taylor et al., 2017). The development and utilization of a national registry for housing newborn screening data may improve monitoring and follow-up of individuals with heritable disorders (U.S. Department of Health and Human Services, 2012; Department of Health and Human Services, 2010).

The Academy's Position

This policy recommendation is aligned with the 2014 to 2017 American Academy of Nursing's Strategic Goal (2.2) to support access to health care services and promote healthy communities and populations. The Academy supports efforts to standardize newborn screening to include minimally, all 34 conditions in the RUSP, and 26 secondary conditions. Further, for state newborn screening programs that will include whole exome or genome sequencing, the screening should include reporting and tracking of the ACMG's 59 actionable variants across all states.

As a national health priority focused on improving population health, the ability to provide continuity of care for vulnerable individuals over their lifespan can be improved by creating a system to connect newborn screening results to a national newborn screening registry that parallels the electronic birth registration system. The Academy supports the recommendation to develop a nationally based newborn screening registry to improve follow-up and contact of screened newborns and families across all states.

The Academy will collaborate with the U.S. Department of Health and Human Services, State Health Departments, the AAP, and consumer organizations such as Genetic Alliance and Baby's First Test, to support the universal implementation of the RUSP panel. The Academy also supports the efforts of the AAP to promote a national electronic registry for tracking and follow up of newborn genetic screening results, as well as the role of nurses in care of families with children affected by these conditions.

Recommendations

1. Make the provision of federal funding to state public health departments dependent upon RUSP implementation to ensure that each state is minimally screening for all 34 core conditions and 26 secondary conditions. Congress should mandate funding mechanisms to state health departments to ensure that each state is carrying out, at a minimum, the RUSP as a quality indicator of how funding is being used.
2. Inform and advocate for change at the local level by raising issues on newborn screening to state public health departments and the state governor's council. Nurses, nurse practitioners, and certified nurse midwives who reside in states that are not meeting RUSP recommendations should meet with their state health departments and governor's council to advocate for RUSP adoption, ensuring equal access and coverage of newborn screening.
3. Advocate to the Secretary of the U.S. Department of Health and Human Services (DHHS) to reconsider the recommendations from the DACHDNC concerning the creation of a field for an NDBS serial number to each birth certificate in the EBRS in order to ensure timely, high-quality screening.
4. Encourage Congress to authorize and appropriate funding to the National Health Statistics and Information System and Nation Center for Health Statistics for development of a national screening registry for follow-up of positive genetic screening results.
5. Urge the collaboration among DHHS, National Health Statistics and Information System, and National Center for Health Statistics Newborn screening programs to ensure the capability of housing genome-wide data with safeguards for ensuring privacy and confidentiality.
6. Advocate for immediate action to develop a national database that incorporates a process to document reporting and tracking of all 59 actionable variants in all state newborn screening programs that will include exome and genome sequencing in collaboration with the DHHS. Incorporation of privacy protections to access the national registry is paramount. However, access to such a database by licensed genetic counselors and health care providers is important for improving the health of America's children and in helping families mitigate health risks that threaten short and longer-term health outcomes.
7. Increase the role of nurses, nurse practitioners, and certified nurse midwives in the process of newborn screening, including working with families for

interpretation of genetic screening results, appropriate referral, and coordination of care.

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