Spinal muscular atrophy was nominated for addition to the RUSP and sent for an evidence-based review in 2017. In February 2018, the Evidence Review Group (ERG), funded under a Health Resources and Services Administration (HRSA) contract, presented its findings to the Committee (ERG 2018, refer to Appendix D for a link to the full report). The Committee voted to recommend to the Secretary that a specific type of SMA, SMA due to homozygous deletion of exon 7 in the SMN1 gene, be added to the RUSP.

In July 2018, the Secretary accepted the Committee's recommendation and approved the addition of this SMA type to the RUSP. Additional details regarding the Committee's recommendation and the Secretary's response are summarized in Appendix C.

3.1.2 Steering Committee

In addition to these activities, the Committee established a steering committee to evaluate the evidence-based review process. A description of the steering committee's planned roles and obligations is presented in Section 4.

3.2 Technical Assistance and Nomination Review

> The Advisory Committee shall
> (4) provide technical assistance, as appropriate, to individuals and organizations regarding the submission of nominations to the uniform screening panel, including prior to the submission of such nominations
> (5) take appropriate steps, at its discretion, to prepare for the review of nominations prior to their submission, including for conditions for which a screening method has been validated but other nomination criteria are not yet met, in order to facilitate timely action by the Advisory Committee once such submission has been received by the Committee

During the 2018 calendar year, the Committee provided technical assistance regarding two conditions nominated to the RUSP:

- Guanidinoacetate methyltransferase (GAMT) deficiency. Guanidinoacetate methyltransferase deficiency is an inherited disorder that affects the nervous system and muscles and can lead to intellectual disability, impairments in speech development, and epilepsy.

  The condition was nominated for addition to the RUSP in 2016; in 2017, the Committee voted not to request an evidence-based review of the condition based on the lack of pilot study data and formalized treatment guidelines. The Committee provided technical assistance to the nominators and described what type of data is needed for the Committee to reconsider the nomination.

  In May 2018, the Committee requested an update from the Centers for Disease Control and Prevention (CDC) as well as comments from public stakeholders (Cuthbert 2018) on progress in GAMT deficiency screening. The Committee is continuing to follow efforts and progress in the field.
- Cerebrotendinous xanthomatosis (CTX). Cerebrotendinous xanthomatosis is an inherited disorder that impairs cholesterol and bile acid metabolism. This disorder results in systemic and neurologic abnormalities, including cerebellar ataxia, juvenile cataracts, chronic diarrhea, neurological deficits, and skin lesions.

3.5.4 Availability and Reporting of Testing

> (D) the availability and reporting of testing for conditions for which there is no existing treatment, including information on cost and incidence

The Committee did not undertake activities relating to the availability or reporting of testing for conditions for which there is no existing treatment during the 2018 calendar year.

3.5.5 Conditions Not Included in the RUSP

> (E) conditions not included in the recommended uniform screening panel that are treatable with Food and Drug Administration-approved products or other safe and effective treatments, as determined by scientific evidence and peer review

The Committee heard an update on the status of GAMT deficiency screening and considered the nomination of CTX (Section 3.2).

3.5.6 Minimum Standards and Related Policies and Procedures

> (F) minimum standards and related policies and procedures used by State newborn screening programs, such as language and terminology used by State newborn screening programs to include standardization of case definitions and names of disorders for which newborn screening tests are performed

In 2018, the Committee heard presentations relating to a resource for newborn screening laboratories developed by the Association of Public Health Laboratories (APHL; Orsini 2018, Bocchini 2018, Kelm 2018). The resource provides an overview of cutoff determinations and risk assessment methods used in dried blood spot newborn screening, including approaches used for risk assessment, factors to consider when establishing and evaluating risk, and instructions on monitoring and evaluating risk assessment and re-evaluating cutoffs (APHL 2018). Committee discussions were one of the catalysts for the development of this resource. The Committee provided feedback during the development of the resource, and the APHL distributed the document to the newborn screening community soliciting feedback in January 2018. A revised final resource is now available through the APHL. The Committee discussed further ways to provide guidance, support, education, and recommendations relating to cutoff determinations and convened an ad-hoc workgroup focused on newborn screening result interpretation (refer to Section 4 for additional details).

3.5.7 Quality Assurance, Oversight, and Evaluation

> (G) quality assurance, oversight, and evaluation of State newborn screening programs, including ensuring that tests and technologies used by each State meet established standards for detecting and reporting positive screening results

In 2018, the Committee heard a presentation from the CDC relating to its quality assurance and harmonization activities (Petritis 2018). The Biochemical Mass Spectrometry Laboratory (BMSL) at the CDC develops first-and second-tier screening assays, conducts hands-on mass spectrometry training, develops and characterizes quality assurance materials, and provides technical assistance to newborn screening laboratories. In addition, the BMSL provides normalized cutoffs and proficiency testing materials that allow newborn screening programs to compare their laboratory cutoffs with those from other laboratories. Together, these activities enhance the consistency and quality of laboratory newborn screening assessments. Additional

work in this area is ongoing as the CDC works to create materials for educational purposes, build an interface for result visualization, and expand the project to cover additional analytes. In response to the presentation, the Committee discussed the potential importance of harmonizing both case definitions and methods for reporting/communicating abnormal screening results nationwide.

Additional Committee activities relating to quality assurance, oversight, and evaluation are described in Section 3.5.6 (APHL cutoff determinations document) and Section 3.5.12 (timeliness initiatives).

3.5.8 Public and Provider Awareness and Education

(H) public and provider awareness and education

In 2018, the Committee finalized a Communication Guide and Educational Planning Guide developed by the Committee's Education and Training Workgroup.

- Communication Guide: This tool is a document that contains guidance for physicians discussing out-of-range newborn screening results and other relevant medical information with parents. It allows physicians to verify a family's comprehension level and provides support during development of a follow-up plan (ACHDNC 2018b, refer to Appendix D for a link to the guide).
- Educational Planning Guide: This tool consists of a matrix that matches newborn screening content areas and educational components with the stakeholders who may need specific information. Its goal is to facilitate creation of newborn screening educational materials tailored to the needs of different stakeholders.

The Committee discussed the most effective strategies for disseminating the tools to the intended end users and evaluating their effectiveness.

In 2018, the Committee also supported the development of consumer-directed summaries of evidence-based review reports for RUSP-nominated conditions. These summaries, funded by HRSA, are intended to help consumers and advocacy groups understand the results of the evidence-based review reports. In 2018, consumer-directed summaries were finalized for the evidence-based review reports for Critical Congenital Heart Disease, Hemoglobin H Disease, Neonatal Hyperbilirubinemia, Krabbe Disease, Mucopolysaccharidosis Type I, Pompe Disease, Severe Combined Immunodeficiency, and X-linked Adrenoleukodystrophy. A consumer-directed summary is being completed for the SMA evidence-based review report. Feedback on the summaries was obtained from individuals with and without expertise in newborn screening to ensure accuracy and readability for a lay audience. All eight completed summaries were posted on the Committee's website alongside the full evidence-based review reports (a link to this page on the Committee's website is available here). The current version of the SMA evidence-based review report summary is provided in Appendix E.

The Committee also heard multiple presentations relating to education in 2018. A representative from Baby's First Test (Newborn Screening Clearinghouse Program funded by HRSA), an organization that informs and supports families and healthcare professionals throughout the newborn screening experience, described to the Committee new tools and initiatives available to the newborn screening community (e.g., an updated website, mobile application, educational materials in Spanish; Bonhomme 2018). In addition, evaluations of these resources by various

stakeholders were presented alongside key takeaways and implications. The Committee also heard presentations by a panel of experts from different institutions highlighting the role of education in newborn screening (Tarini 2018). The panel featured achievements and ongoing activities in newborn screening education, including a report on the Education and Engagement Summit held in Washington, DC in June 2017, development of new educational tools, and use of a deliberative community engagement process in newborn screening education.

3.5.9 Cost and Effectiveness

> (I) the cost and effectiveness of newborn screening and medical evaluation systems and intervention programs conducted by State-based programs

Beginning in 2015, the Committee's Cost Analysis Workgroup reviewed methods for assessing and estimating the costs of newborn screening expansion. As of 2018, all evidence-based reviews (including the review of SMA completed in 2018) include an estimate of the cost to the state of adding a nominated and reviewed condition to the state's newborn screening panel. For more information on the SMA evidence-based review, refer to Section 3.1.

3.5.10 Causes, Public Health Impacts, and Risk Factors

> (J) identification of the causes of, public health impacts of, and risk factors for heritable disorders

In 2018, the Committee heard two presentations relating to the public health impacts of heritable disorders.

One panel presentation by experts from different institutions examined the ethical, legal, social, and policy considerations of using genomic sequencing in newborn screening (Powell 2018). Next-generation genomic sequencing tools and technology are rapidly evolving, and their incorporation into newborn screening paradigms is anticipated. However, the use of such tools in newborn screening raises complex ethical, legal, social, and policy issues. Whole-genome sequencing is generally not recommended as a sole screen in newborns, but targeted sequencing as a confirmatory test has been utilized successfully for some conditions. The presenters recommended obtaining additional data, particularly on the harms and benefits of using genomic sequencing in newborn screening.

The Committee also heard a presentation on methods for incorporating ethical, legal, and social implications (ELSI) research questions into newborn screening pilot studies (Brosco 2018). Considerations relating to ELSI are complex for RUSP-nominated conditions. One approach, implemented by the Parent Project Muscular Dystrophy ELSI Workgroup, categorizes ELSI issues into two main categories: those related to the results of newborn screening and those related to the initiation and implementation of newborn screening at the systems level. Based on the experience of the workgroup, it was recommended that the Committee and future nominators consider possible ways to integrate ELSI-related questions into pilot studies for RUSP-nominated conditions. Inclusion of such questions would better define the benefits and harms of the nominated conditions, delineate the potential impact of screening for the conditions, and potentially improve policymaker decisions.

3.5.11 Coordination of Surveillance Activities

> (K) coordination of surveillance activities, including standardized data collection and reporting, harmonization of laboratory definitions for heritable disorders and testing results,

and confirmatory testing and verification of positive results, in order to assess and enhance monitoring of newborn diseases

The Committee did not undertake activities relating to the coordination of surveillance activities during the 2018 calendar year.

3.5.12 Timeliness of Collection, Delivery, Receipt, and Screening

(L) the timeliness of collection, delivery, receipt, and screening of specimens to be tested for heritable disorders in newborns in order to ensure rapid diagnosis and follow-up

The Committee developed goals for timeliness in collecting and delivering newborn screening specimens to laboratories as well as in reporting results (ACHDNC 2017). In 2018, the Committee heard presentations on approaches to achieving timeliness goals from state newborn screening programs in Oklahoma, Arizona, and Iowa (Aponte 2018, Berberich 2018, McCallister 2018). Representatives from each state described specific initiatives for meeting the timeliness goals (e.g., improving transit time efficiencies, educating key personnel, adjustments in laboratory schedules) along with the results of these initiatives. After hearing from the representatives, the Committee discussed the resources needed for states to achieve timeliness goals and the value of reporting the results of timeliness initiatives to the public.

In 2018, the Committee also heard a presentation from NewSTEPs 360 (a HRSA-funded initiative focused on improving timeliness within newborn screening) describing a variety of ongoing projects directed toward timeliness (Sontag 2018). These projects included quality improvement coaching, an online data repository, a continuous quality improvement framework, annual in-person meetings, technical and financial assistance, webinars, and tools to monitor progress and change. In addition, successes from the 2014-2015 NewSTEPs 360 Mini-Collaborative Improvement and Innovation Network and subsequent newborn screening timeliness quality improvement initiative, which involved coordination of in-person meetings and skill-building sessions, were reported. Finally, the Committee heard about a timeliness toolkit developed by NewSTEPs 360 in collaboration with the March of Dimes and Association of State and Territorial Health Officials that can help state newborn screening programs work toward expansion of courier service and operating hours.

4 FUTURE DIRECTIONS

The Committee will support the following ongoing projects expected to continue through or be finalized in 2019:

- Examination of newborn screening result interpretation. An ad-hoc workgroup focused on interpreting newborn screening results was established in 2018. This cross-functional, multidisciplinary workgroup includes Committee members and experts serving on the Committee's Education and Training and Laboratory Standards and Procedures Workgroups. Growing from the need to educate stakeholders on the strengths and limitations of newborn screening results, it will consider methods for interpreting screening results and provide recommendations on cutoff establishment and monitoring. In 2019, the workgroup will communicate with key partners in the newborn screening community and develop and disseminate its findings.
- Continued assessment of the public health impact of adding conditions to the RUSP. The Newborn Screening Saves Lives Reauthorization Act requires that evidence-based reviews evaluate the public health impact of RUSP expansion. The ERG, in collaboration with the APHL, has developed tools (e.g., webinars, surveys, follow-up interviews) for evaluating this impact, and refinement of these tools will continue in 2019.
- Continued development and refinement of educational tools, including the Educational Planning Guide.
- Completion and dissemination of the consumer-directed summary of the evidence-based review report for SMA.

In addition, the Committee expects to initiate the following new projects in 2019:

- Re-examination of the evidence-based review process. Beginning in 2019, an expert panel that includes Committee members, ERG members, and others will evaluate potential changes in the current overall review process, revisions to the decision matrix, assessment of the public health impact, costs, and methods for nominating conditions for removal from the RUSP.
- Retrospective review of the implementation of conditions added to the RUSP since 2008. Beginning in 2019, the Committee will examine how implementation of conditions added to the RUSP has been accomplished. Topics to be evaluated include the accuracy of estimated time frames, unanticipated challenges, and clinical and public health implications of adding conditions with delayed onset and variable severity.
- Review of newborn SMA screening implementation and clinical outcomes of early SMA treatment, as requested by the Secretary of Health and Human Services. This project will begin in 2019 and conclude with a final report in 2020.
- Review and analysis of newborn screening timeliness initiatives and outcomes. This project will begin in 2019 and last through 2020.

5 CONCLUSIONS

This report was prepared to summarize the Committee's activities and outcomes for the 2018 calendar year and to fulfill the legislative requirement for the submission of an annual report on the Committee's activities to Congress, the Secretary, the Interagency Coordinating Committee on Newborn and Child Screening, and the state health departments. The mission of the Committee is to reduce morbidity and mortality in newborns and children who have, or who are at risk for, genetic disorders. It accomplishes this mission by providing advice, recommendations, and technical information to the Secretary of the Department of Health and Human Services and helping to develop policies and priorities meant to enhance services at the state and local levels. In addition, it invites public comments as an important way to identify issues and concerns relating to newborn screening.

In 2018, the Committee continued to make systematic, evidence-based, and peer-reviewed recommendations on conditions for which all newborns should be screened. The Committee completed activities relating to three conditions nominated to the RUSP: review of the CTX nomination, provision of guidance on the GAMT deficiency nomination, and completion of the SMA evidence-based review and subsequent recommendation to add SMA to the RUSP. In addition, the Committee prepared for continuing refinement of the evidence-based review process in the next calendar year.

The Committee also continued to serve in a leadership role in the field of newborn screening and genetic disorders by supporting efforts to improve data quality and processes. In 2018, it issued formal reports on key newborn screening topics, developed educational resources targeted to specific stakeholders within and outside of the newborn screening community, and maintained involvement in areas of active development in the field, including timeliness, standard and procedure development, application of new technology, and ethics.

The coordinated efforts of the Committee and stakeholders—including policymakers, state public health agencies, providers, and the public—will continue to ensure that newborns and children have universal access to high-quality screening, follow-up, diagnosis, disease management and treatment, evaluation, and education. Together, these efforts will continue to reduce or prevent the potentially devastating consequences of disabilities, life-threatening diseases, or death.

6 REFERENCES

Advisory Committee on Heritable Disorders in Newborns and Children website. https://www.hrsa.gov/advisory-committees/heritable-disorders/index.html. Updated November 2018. Accessed December 1, 2018.

Advisory Committee on Heritable Disorders in Newborns and Children. Communication Guide. https://www.hrsa.gov/sites/default/files/hrsa/advisory-committees/heritable-disorders/reports-recommendations/reports/achdnc-communication-guide-newborn.pdf. Accessed December 1, 2018.

Aponte S. Arizona Newborn Screening Timeliness: A 5 Year Summary. Oral presentation at: The Advisory Committee on Heritable Disorders in Newborns and Children Meeting; May, 2018; Rockville, MD.

Berberich SL. Timeliness in NBS: The Iowa Perspective. Oral presentation at: The Advisory Committee on Heritable Disorders in Newborns and Children Meeting; May, 2018; Rockville, MD.

Bocchini JA. Cutoffs and Risk Assessment in Newborn Screening. Oral presentation at: The Advisory Committee on Heritable Disorders in Newborns and Children Meeting; May, 2018; Rockville, MD.

Bonhomme N. Baby's First Test: What is offered, Who we Reached, What we've Learned. Oral presentation at: The Advisory Committee on Heritable Disorders in Newborns and Children Meeting; November, 2018; Rockville, MD.

Brosco JP. Including ELSI research questions in newborn screening pilot studies. Oral presentation at: The Advisory Committee on Heritable Disorders in Newborns and Children Meeting; November, 2018; Rockville, MD.

Cuthbert C. Update on Newborn Screening for Guanidinoacetate Methyltransferase (GAMT) Deficiency. Oral presentation at: The Advisory Committee on Heritable Disorders in Newborns and Children Meeting; May, 2018; Rockville, MD.

Evidence Review Group. Evidence-Based Review of Newborn Screening for Spinal Muscular Atrophy (SMA): Final Report (v5.2). https://www.hrsa.gov/sites/default/files/hrsa/advisory-committees/heritable-disorders/reports-recommendations/sma-final-report.pdf. Published March 13, 2018. Accessed December 1, 2018.

Follow-Up and Treatment Workgroup. The Role of Quality Measures to Promote Long-Term Follow-up of Children Identified by Newborn Screening Programs. https://www.hrsa.gov/sites/default/files/hrsa/advisory-committees/heritable-disorders/reports-recommendations/reports/role-of-quality-measures-in-nbs-sept2018-508c.pdf. Published February 8, 2018. Accessed December 1, 2018.

Kelm K. Risk Assessment in Newborn Screening. Oral presentation at: The Advisory Committee on Heritable Disorders in Newborns and Children Meeting; August, 2018; Rockville, MD.

Kemper AR. Long-Term Follow-up After Newborn Screening: Environmental Scan. Oral presentation at: The Advisory Committee on Heritable Disorders in Newborns and Children Meeting; August, 2018a; Rockville, MD.

Kemper AR. Newborn Screening Technology: A Compendium Resource. Oral presentation at: The Advisory Committee on Heritable Disorders in Newborns and Children Meeting; August, 2018b; Rockville, MD.

McCallister T. Newborn Screening Timeliness in Oklahoma. Oral presentation at: The Advisory Committee on Heritable Disorders in Newborns and Children Meeting; May, 2018; Rockville, MD.

Orsini J. Overview of Cutoff Determinations and Risk Assessment Methods used in Dried Blood Spot Newborn Screening. Oral presentation at: The Advisory Committee on Heritable Disorders in Newborns and Children Meeting; February, 2018; Rockville, MD.

Overview of Cutoff Determinations and Risk Assessment Methods used in Dried Blood Spot Newborn Screening (Association of Public Health Laboratories website). https://www.aphl.org/programs/newborn_screening/Documents/Overview%20on%20Cutoff%20Determinations%20and%20Risk%20Assessment%20Methods%20used%20in%20NBS.pdf. Accessed December 1, 2018.

Petritis K. CDC's Quality Assurance and Harmonization Activities. Oral presentation at: The Advisory Committee on Heritable Disorders in Newborns and Children Meeting; May, 2018; Rockville, MD.

Powell CM. An Introduction to Genomic Sequencing in Newborn Screening: Ethical, Legal, and Social Implications. Oral presentation at: The Advisory Committee on Heritable Disorders in Newborns and Children Meeting; November, 2018; Rockville, MD.

Public Health Service Act. 42 United States Code § 300b–10 (2014).

Newborn Screening Timeliness Goals (Advisory Committee on Heritable Disorders in Newborns and Children website). https://www.hrsa.gov/advisory-committees/heritable-disorders/newborn-screening-timeliness.html. Updated September 2017. Accessed December 1, 2018.

Sontag M. Improving Timeliness in Newborn Screening: The Story Behind the Story. Oral presentation at: The Advisory Committee on Heritable Disorders in Newborns and Children Meeting; August, 2018; Rockville, MD.

Tarini B. Education Activities Panel. Oral presentation at: The Advisory Committee on Heritable Disorders in Newborns and Children Meeting; November, 2018; Rockville, MD.

7 APPENDICES

Appendix A: Membership of the Advisory Committee on Heritable Disorders in Newborns and Children

The Secretary of Health and Human Services (or his/her designee) appoints members to the Committee. The Committee may include up to 15 voting members, including the Chair and federal ex-officio members, as well as up to 15 nonvoting organizational representatives, as the Secretary determines necessary. In addition, a Designated Federal Official from the Health Resources and Services Administration's Maternal and Child Health Bureau serves as the government's agent for matters related to the management of the Committee's activities. This individual ensures that all procedures are within applicable statutory, regulatory, and Health and Human Services General Administration Manual directives. The following is a list of the Committee members who served in 2018.

Members

- **Mei Wang Baker, MD**
  Professor of Pediatrics University of Wisconsin School of Medicine and Public Health
  Co-Director, Newborn Screening Laboratory
  Wisconsin State Laboratory of Hygiene
  Term End Date: June 30, 2020
- **Susan A. Berry, MD**
  Professor and Director
  Division of Genetics and Metabolism
  Departments of Pediatrics and Genetics, Cell Biology & Development
  University of Minnesota
  Term End Date: June 30, 2021
- **Joseph A. Bocchini, Jr., MD (Chairperson)**
  Professor and Chairman
  Department of Pediatrics Louisiana State University
  Term End Date: April 24, 2019
- **Jeffrey P. Brosco, MD, PhD**
  Professor of Clinical Pediatrics
  University of Miami School of Medicine Department of Pediatrics
  Deputy Secretary, Children's Medical Services Florida State Department of Health
  Term End Date: June 30, 2020
- **Dietrich Matern, MD, PhD**
  Professor of Laboratory Medicine, Medical Genetics, and Pediatrics
  Mayo Clinic
  Term End Date: June 30, 2018

- **Cynthia M. Powell, MD**
  Professor of Pediatrics and Genetics
  Director, Medical Genetics Residency Program
  Pediatric Genetics and Metabolism
  The University of North Carolina at Chapel Hill
  Term End Date: June 30, 2021
- **Annamarie Saarinen**
  Co-founder, CEO
  Newborn Foundation
  Term End Date: June 30, 2020
- **Scott M. Shone, Ph.D., HCLD(ABB)**
  Senior Research Public Health Analyst
  RTI International
  Term End Date: June 30, 2021
- **Beth Tarini, MD, MS, FAAP**
  Associate Professor and Division Director
  General Pediatrics & Adolescent Medicine
  University of Iowa Hospitals & Clinics
  Term End Date: June 30, 2020
- **Catherine A. L. Wicklund, MS, CGC**
  Northwestern University Feinberg School of Medicine
  Center for Genetic Medicine
  Term End Date: June 30, 2018

Ex-Officio Members

- **Agency for Healthcare Research and Quality**
  Kamila B. Mistry, PhD, MPH
  Senior Advisor
  Child Health and Quality Improvement
- **Centers for Disease Control and Prevention**
  Carla Cuthbert, PhD
  Chief, Newborn Screening and Molecular Biology Branch
  National Center for Environmental Health
- **Food and Drug Administration**
  Kellie B. Kelm, PhD
  Deputy Director
  Division of Chemistry and Toxicology Devices
  Office of In Vitro Diagnostics and Radiological Health
- **Health Resources and Services Administration**
  Laura Kavanagh, MPP
  Acting Associate Administrator
  Maternal and Child Health Bureau

- **National Institutes of Health**
  Diana W. Bianchi, MD
  Director
  Eunice Kennedy Shriver National Institute of Child Health and Human Development

Designated Federal Official

- **Catharine Riley, PhD, MPH**
  Health Resources and Services Administration
  Maternal and Child Health Bureau

Appendix E: Consumer-Directed Summary of the Evidence-Based Review Report for SMA

After the completion of evidence-based review reports for conditions nominated to the RUSP, summaries of the full reports are created for the general public. Each summary outlines the key points of the evidence-based review report and includes a description of the Committee's discussion and whether the condition was added to the RUSP. The summaries are targeted to a range of audiences, including the general public as well as specific stakeholders (e.g., parents, advocates, state public health programs, and policy decision-makers). Each final summary is no longer than ten pages and is accompanied by a one-page executive summary.

Consumer-directed summaries were developed or finalized for the following nine conditions in 2018: X-linked Adrenoleukodystrophy, Mucopolysaccharidosis Type I, Pompe Disease, Severe Combined Immunodeficiency, Krabbe Disease, Neonatal Hyperbilirubinemia, Hemoglobin H Disease, Critical Congenital Heart Disease, and SMA. Completed summaries are posted on the Committee website.

An example consumer summary of the external evidence-based review report for SMA is provided below.

ABOUT THIS SUMMARY

What is newborn screening?

Newborn screening is a public health service that can change a baby's life. Newborn screening involves checking all babies to identify those few who look healthy but who are at risk for one of several serious health disorders that benefit from early treatment.

Certain serious illnesses can be present even when a baby looks healthy. If the baby does not receive screening for these illnesses early in life, a diagnosis may be delayed. Treatment started later might not work as well as earlier treatment. Newborn screening programs have saved the lives and improved the health of thousands of babies in the United States (US).

Who decides what screening newborns receive?

In the US, each state decides which disorders to include in its newborn screening program. To help states determine which disorders to include, the US Secretary of Health and Human Services provides a list of disorders recommended for screening. This list is called the Recommended Uniform Screening Panel (RUSP).

Progress in screening and medical treatments can lead to new opportunities for newborn screening. To learn how a disorder is added to the RUSP, see **Box A**.

What will this summary tell me?

In 2017, the Advisory Committee on Heritable Disorders in Newborns and Children (ACHDNC) requested an evidence review of newborn screening for spinal muscular atrophy (SMA). This summary presents key review information that the Committee used to make its decision about whether to recommend adding SMA to the RUSP. It will answer these questions:

- What is SMA?
- How is SMA treated?
- How are newborns screened for SMA?
- Does early diagnosis or treatment help patients with SMA?
- What is the public health impact of newborn SMA screening in the US?
- Did the Committee recommend adding SMA to the RUSP?

Box A: Adding a Disorder to the RUSP

A committee, called the Advisory Committee on Heritable Disorders in Newborns and Children (ACHDNC), makes a recommendation to the US Secretary of Health and Human Services about adding specific disorders to the RUSP. The Committee bases its decision on a review of the disorder, the screen, the treatment, and the ability of newborn screening programs to check for the disorder. To learn more about the ACHDNC, visit this website.

UNDERSTANDING THE DISORDER

What is SMA?

SMA is a rare genetic disorder. People with SMA have a change in a gene called *SMN1*. Normally, this gene makes a protein that allows healthy nerves to control muscles in the body. In people with SMA, part of the *SMN1* gene is missing, and the gene does not make as much of the protein as normal. Some people with SMA can make enough of this protein with a related gene called *SMN2*. However, the *SMN2* gene does not always produce enough of the protein to keep nerve cells healthy. As a result, nerve cells that control muscles may not work correctly, causing serious health problems that, without treatment, can lead to death in the first months or years of life.

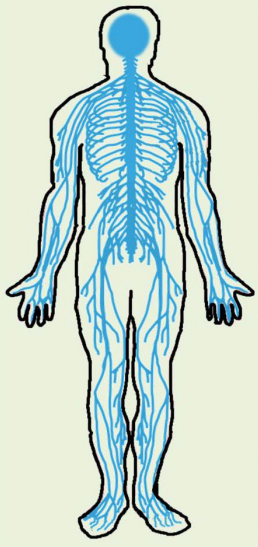
How common is SMA?

- SMA is a rare disorder. About 1 out of every 11,000 people receives a diagnosis of SMA.
- This estimate is based on the number of people who develop symptoms and receive a diagnosis without newborn screening.

What kinds of health problems does SMA cause?

SMA damages the nerve cells that carry messages from the brain to the muscles of the body (Figure 1). This causes muscle weakness and leads to difficulty with many important actions. SMA does not affect nerves involved in sensation, thinking, or learning.

Figure 1: SMA Symptoms.



Movement problems
SMA can damage nerve cells carrying messages from the brain to the skeletal muscles. This causes problems with actions like turning the head, sitting, crawling, and walking.

Breathing problems
SMA can damage nerve cells carrying messages from the brain to the muscles used for breathing. This causes problems with lung development, normal and effective breathing, coughing, and infections.

Other problems
SMA can damage nerve cells carrying messages from the brain to other important muscles. For example, damage to the muscles used for swallowing causes difficulty with safe swallowing, reflux, and heartburn. SMA does not affect the nerve cells involved in sensation, thinking, or learning.

What are some of the benefits and risks of newborn SMA screening?

Table 2 describes the benefits and risks of newborn SMA screening as of 2018.

Table 2: Benefits and Risks of Screening.

Benefits	Risks
• Earlier identification and diagnosis of babies with SMA.	• Screening and follow-up testing require taking blood, which can cause pain. • The timing and type of problems caused by SMA can be hard to predict based on screening and follow-up testing.
• Earlier treatment, which might improve motor function and survival.	• Earlier exposure to the possible risks of treatment. • Some babies with SMA detected through newborn screening may not need treatment right away.
• More time to plan for the future.	• Screening and follow-up testing cannot always predict the type of SMA a newborn has. This might cause more anxiety about the future.
• Health counseling and family planning for family members.	• Sometimes, people do not want to know genetic risks. Some families do not like sharing health information.

Does early diagnosis or treatment help patients with SMA?

Early diagnosis allows **early monitoring and treatment**, which seem to improve outcomes for people with SMA. Some research suggests that early treatment (when

treatment begins before symptoms develop) improves motor outcomes and lowers the risk of death or needing a ventilator in people with SMA.

Experts need to learn more before they can say for sure that early treatment helps in SMA.

Box B: Where Can I Learn More?

Follow the links below to learn more about information from this summary.

- To learn more about SMA, visit the National Institutes of Health SMA website.
- Visit the Committee's website to learn more about:
  - Nominating conditions to the RUSP.
  - The full SMA evidence report.
  - The ACHDNC recommendation to the Secretary to add SMA to the RUSP.

PUBLIC HEALTH IMPACT

How would newborn SMA screening affect the health of the country?

Based on what is known about screening and the risk of being born with SMA, experts think that screening all newborns in the US for SMA would do the following:

- Find about 364 babies with SMA each year.
- Prevent between 16 and 100 children with SMA Type 1 from needing a ventilator each year.
- Prevent between 14 and 68 deaths due to SMA Type 1 each year.

Without screening, diagnosing SMA can take time because most babies with SMA will not have symptoms right away. Newborn screening for SMA allows diagnosis in the first weeks of life (even if a baby has no symptoms), when treatment may be most effective.

What is the status of newborn SMA screening in the US?

- At the time of the 2018 evidence review, 2 states (Massachusetts and Utah) screened newborns for SMA. Two more states (Minnesota and Missouri) had mandates to start screening for SMA.
- Most states estimated that implementing newborn SMA screening would take 1 to 3 years.

ADVISORY COMMITTEE DECISION

What did the Committee recommend?

The Committee voted in 2018 to recommend adding SMA to the RUSP. The Committee based its decision on the ability of screening to find babies with SMA and evidence that early treatment was better than later treatment. In 2018, the US Secretary of Health and Human Services recommended that all newborns receive SMA screening.

To screen for any disorder, states must be prepared. They must have the right equipment and procedures. There must also be specialists who can work with families to determine whether a baby has the disorder and, if so, the best treatment.

HELPFUL INFORMATION

Glossary

Term	Definition
ACHDNC	Advisory Committee on Heritable Disorders in Newborns and Children. The committee that oversees the RUSP.
Dried blood spot	A drop of blood that is collected from a baby's heel, dried onto a special piece of paper, and used to screen for many disorders.
Gene therapy	A type of treatment for SMA that replaces or corrects the *SMN1* gene.
Nusinersen	A treatment for SMA that can stop SMA problems from getting worse.
SMA	Spinal muscular atrophy. A rare disorder affecting the nerves that control muscles of the body.
RUSP	Recommended Uniform Screening Panel. The list of disorders recommended for newborn screening.
Secretary of Health and Human Services	The head of the US Department of Health and Human Services. This person decides whether to add disorders to the RUSP.
SMN1	The gene responsible for causing SMA. In people with SMA, part of this gene is missing.
SMN2	A gene similar to *SMN1* that is targeted in SMA treatment.
Specialist	A doctor with expertise in a specific area of medicine.
Ventilator	A machine that helps with breathing.

Source

The information in this summary comes from the report *Evidence-Based Review of Newborn Screening for Spinal Muscular Atrophy (SMA): Final Report (v5.2)* (13 March 2018), commissioned by the ACHDNC. The report reviewed evidence on SMA screening and treatments in children through January 2018. It included both published and unpublished research. To see a copy of the report, visit this page.