Advisory Committee on Heritable Disorders in Newborns and Children

Meeting Summary
August 2, 2018

The Advisory Committee on Heritable Disorders in Newborns and Children (Committee) meeting was convened on August 2, 2018 and adjourned on August 2. In accordance with the provisions of Public Law 92-463, the meeting was open for public comment.

Committee Members

Mei Baker, M.D.
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Co-Director, Newborn Screening Laboratory
Wisconsin State Laboratory of Hygiene

Susan A. Berry, M.D.
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Department of Pediatrics and Genetics
Cell Biology & Development
University of Minnesota

Joseph A. Bocchini, Jr., M.D. (Chairperson)
Professor and Chairman
Department of Pediatrics
Louisiana State University

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Scott M. Shone, Ph.D.
Senior Research Public Health Analyst
RTI International

Beth Tarini, M.D., M.S., FAAP
Associate Professor and Division Director
General Pediatrics & Adolescent Medicine
University of Iowa Hospitals & Clinics

Ex-Officio Members

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Centers for Disease Control & Prevention
Carla Cuthbert, Ph.D.
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Food and Drug Administration
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Health Resources & Services Administration
Laura Kavanagh, MPP
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Designated Federal Official

Catharine Riley, Ph.D., M.P.H.
Health Resources and Services Administration
Genetic Services Branch
Maternal and Child Health Bureau

Organizational Representatives

American Academy of Family Physicians
Robert Ostrander, M.D.
Valley View Family Practice

American Academy of Pediatrics
Debra Freedenberg, M.D., Ph.D.
Texas Department of State Health Services

American College of Medical Genetics
Michael S. Watson, Ph.D., FACMG
Executive Director

American College of Obstetricians & Gynecologists
Britton Rink, M.D., M.S.
Mount Carmel Health Systems

Association of Maternal & Child Health Programs
Jed Miller, M.D.
Director, Office of the Office for Genetics and People with Special Health Care Needs
Maryland Department of Health Maternal and Child Health Bureau

Association of Public Health Laboratories
Susan M. Tanksley, Ph.D.
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Department of Pediatrics, MCHK-PE Tripler

Genetic Alliance
Natasha F. Bonhomme
Vice President of Strategic Development
Genetic Alliance

March of Dimes
Siobhan Dolan, M.D., M.P.H.
Professor and Vice Chair for Research
Department of Obstetrics & Gynecology and Women's Health
Albert Einstein College of Medicine and Montefiore Medical Center

National Society of Genetic Counselors
Cate Walsh Vockley, M.S., CGC
Senior Genetic Counselor Division of Medical Genetics Children's Hospital of Pittsburgh

Society for Inherited Metabolic Disorders
Carol Greene, M.D.
University of Maryland Medical System
Pediatric Genetics

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I. Administrative Business — August 02, 2018

Joseph A. Bocchini, Jr., M.D.
Committee Chair
Professor and Chairman
Department of Pediatrics
Louisiana State University

Catharine Riley, Ph.D., MPH
Designated Federal Official
Health Resources and Services Administration

A. Welcome and Roll Call

Dr. Bocchini welcomed participants to the third meeting for 2018 of the Advisory Committee on Heritable Disorders in Newborns and Children.

Dr. Bocchini then conducted the roll call. The Committee members in attendance were:

- Dr. Mei Baker
- Dr. Susan Berry
- Dr. Bocchini
- Dr. Jeffrey Brosco
- Dr. Scott Grosse (Centers for Disease Control and Prevention)*
- Dr. Kellie Kelm (Food and Drug Administration)
- Dr. Melissa Parisi (National Institutes of Health)
- Dr. Cynthia Powell
- Ms. Annamarie Saarinen
- Ms. Joan Scott (Health Resources and Services Administration)
- Dr. Scott Shone
- Dr. Beth Tarini
- Dr. Catharine Riley (Designated Federal Official)
- *(Dr. Carla Cuthbert attended for the CDC during the afternoon portion of the meeting)

Organizational representatives in attendance were:

- American Academy of Pediatrics, Dr. Debra Freedenberg
- American College of Medical Genetics, Dr. Michael Watson
- Association of Maternal and Child Health Programs, Dr. Jed Miller
- Genetic Alliance, Ms. Natasha F. Bonhomme
- March of Dimes, Dr. Siobhan Dolan
- National Society of Genetic Counselors, Ms. Cate Walsh-Vockley
- Society for Inherited Metabolic Disorders, Dr. Shawn E. McCandless*
- American Academy of Family Physicians, Dr. Robert Ostrander
- Association of Public Health Laboratories, Dr. Susan Tanksley
- Association of State & Territorial Health Officials, Dr. Chris Kus

*Dr. Bocchini introduced Dr. McCandless as the new organizational representative for the Society for Inherited Metabolic Disorders.

B. Vote on May 2018 Meeting Minutes

By roll call vote, the minutes were approved by all Committee members who were present.

C. SMA Update

Dr. Bocchini updated the Committee on a letter received from the Secretary of Health and Human Services on July 2, 2018, in response to the Committee's recommendation that spinal muscular atrophy (SMA) due to homozygous deletion of exon 7 and SMN1 be added to the Recommended Uniform Screening Panel (RUSP). The Secretary accepted the recommendation and asked the Committee to provide a status report within two years that describes the status of implementation of newborn screening of SMA, including clinical outcomes of early treatment and potential harms for infants diagnosed with SMA. The letter and the full SMA evidence review report are posted on the Committee's website.

D. Organizational Representatives

Noting how valuable organizational representatives' expertise and input are to the Committee, Dr. Bocchini invited organizations to apply for formal representation at Committee meetings through designated organizational representatives. Criteria for selection of organizations are posted on the website and a call will be put out soon to encourage submissions. He announced that applications already received are under consideration.

E. Evidence-Based Review Process

Dr. Bocchini reminded the Committee of its decision to evaluate the condition-nominating process and the establishment of a steering committee to move forward with this review. This review will include options for nominating a condition for addition to the RUSP and removing conditions from the RUSP. The entire condition-review process will also be assessed, including how the evidence review is conducted, relevant components, how evidence is presented to the Committee, and use of the decision matrix. The Committee is working with HRSA to initiate this activity and members will be kept apprised of activities.

F. Implementation of New Conditions to the RUSP

Dr. Bocchini announced the Committee's plan to assess the implementation of conditions that have been added to the RUSP in the last decade, by examining retrospectively how implementations have been carried out, including the accuracy of estimated time frames and unanticipated barriers and challenges to implementation. The Committee will also evaluate the clinical and public health implications of adding conditions with known delayed onset and severity. The Committee is working with HRSA to initiate these efforts.

II. Risk Assessment in Newborn Screening

Kellie Kelm, Ph.D.
Chief, Cardio-Renal Diagnostic Devices Branch
Office of In Vitro Diagnostic Devices Evaluation& Safety
Food and Drug Administration

Dr. Bocchini reminded the Committee that risk assessment in newborn screening is an issue the Committee has discussed for a while. The Laboratory Standards and Procedures Workgroup has been providing feedback on the development of a risk assessment guidance resource for states, led by the Association of Public Health Laboratories (APHL).

Dr. Kelm noted that, after a series of presentations in 2017 related to cutoffs and screening algorithms, APHL began work on its risk assessment guidance document, which was presented to the Laboratory Standards and Procedures Workgroup in August 2017. The Workgroup provided feedback and the draft was shared with the newborn screening community in January 2018 to get additional input. The document describes the scientific processes behind establishing and validating cutoffs and will be a valuable resource for state newborn screening programs. It is intended to be a living document, and thus, will be revised as needed. The guidance document does not include best practices for screening, nor a way to harmonize newborn screening test results across states. The Workgroup and the Advisory Committee provided additional feedback:

- The addition of a summary table that highlights the different types of cutoffs and how they are used.
- Clarity in the section on Collaborative Laboratory Integrated Reports (CLIR)
- More balance in the discussion of the different methods and available technologies

Dr. Kelm reported that the document is close to final; corrections to the section on multiples of the medians need to be added. APHL plans to post the document on its website in the coming weeks.

She then provided an update of CDC activities pertaining to normalization of results from mass spectrometry. She noted that cutoffs may vary among different labs due to many factors including varying extraction methodologies, instrumentation, internal standards, and calibration techniques. CDC is working on harmonization methods by analyzing proficiency testing results to confirm that the normalization process is working. CDC is also working on a web interface to help visualize normalization results. CDC also plans to add additional analytes to the QC materials that will be shipping in early 2019, noting that there are limitations to using proficiency testing samples to confirm that normalization is working.

Dr. Kelm shared NewSTEPs' current activities:

- Communication and outreach
- Quality improvement
- A centralized data repository
- Dynamic data infographics and visualization tools
- HIT framework integration support
- Improving assessments and collection of information on false negatives
- The risk assessment document

She noted that NewSTEPs recently received funding from HRSA for quality improvement projects, one of which involves identification and follow up on out-of-range results. In addition, the NewSTEPs' Technical Assistance Resource Center provides training, addresses challenges, and supports program improvement.

Dr. Kelm reminded the Committee about discussions regarding a possible cross-workgroup effort between the Laboratory Standards and Procedures and Education and Training Workgroups to educate different target audiences on the strengths and limitations of newborn screening results, in particular, providing education to physicians that clinical signs and symptoms ought to be followed up on, regardless of newborn screening results.

She concluded by asking whether there was any change in the Committee's recommendations for what to do with the risk assessment document, and whether the Committee would like to see the proposed cross-Workgroup formed.

A. Discussion

- Would using multiples of the median be a more efficient way to obtain data?
- Dr. Sue Berry, who is involved in the Midwest Genetics Network, noted that the American Board of Pediatrics approved the network's MOC4 educational activity for pediatricians on newborn screening. Members discussed the MOC4 and ways to make it more widely available; eventually, the network hopes to share it with other types of providers.
- Revisions to the APHL document have made it stronger and could help move toward harmonization.
- Committee members commented on the role the Laboratory Standards and Procedures Workgroup could play in collaborating with the Education and Training Workgroup; potentially helping to disseminate the education tools that the Education and Training and other organizations, such as NewSTEPs, APHL and Genetic Alliance are developing.
- Committee members also discussed the media and public attention given to newborn screening, which could provide one avenue for education efforts. A member called for clarification regarding whether the goal is to educate the public generally or change physicians' and parents' behavior.
- There was agreement that we need an understanding of the full landscape of newborn screening education activities and efforts, so gaps and effective strategies to address those gaps can be identified.
- A Committee member cautioned the group about working toward new policies or big initiatives to address what might be a small problem in terms of the numbers of children missed in newborn screening.
- Committee members also discussed just-in-time information for providers and the types of education needed to serve different audiences.
- Should the Committee provide recommendations to programs on what types of information ought to accompany newborn screening results when they are sent to providers?
- How would this information differ from that provided in ACT sheets? An organizational representative indicated physicians will likely not go online to obtain the ACT sheets or refer to white papers or education modules—it would be more effective to provide a short educational "blurb" to send to state laboratories that could be included with newborn screening results.

- A Committee member noted that the primary care physicians who are often on the forefront of educating parents about newborn screening results might require additional guidance and information about newborn screening.
- It was also pointed out that specialty physicians—such as immunologists who diagnose SCID and neurologists who diagnose individuals with SMA—should also be considered.
- It was suggested that the Committee could make recommendations about what types of information should be sent to physicians and stressed that this material should accompany—not be sent separately from—newborn screening results, with the understanding that this information may already exist.
- Organizational representatives highlighted the need to raise awareness among providers that screening tests are not definitive but need to be confirmed and that physicians should be cognizant of symptoms, regardless of newborn screening results. It was also pointed out that physicians need to be reminded about the potential for both false negatives and false positives.

Dr. Bocchini concluded that the Laboratory Standards and Procedures Workgroup should continue to examine the risk assessment document that APHL is refining while the Education and Training Workgroup continues to evaluate the landscape to determine who needs education and what types. An ad hoc workgroup will be considered. The goal will be to work with other groups to coordinate efforts and resources to provide all necessary education to physicians, parents, the public and the media.

III. Improving Timeliness in Newborn Screening: The Story Behind the Story

Marci Sontag, Ph.D.
Director, NewSTEPs 360, Colorado School of Public Health
Director, Center for Public Health Innovation, CI International

Dr. Sontag described the work going on behind the scenes at NewSTEPs 360 and its partner states to address timeliness issues, as well as videos and tools NewSTEPs has developed. Activities include:

- Quality improvement coaching
- An online data repository
- A CQI framework with PDSA cycle
- Annual in-person meetings
- Technical assistance
- Financial assistance
- All-awardee webinars
- Tools to monitor progress and change

She also explained ways the states have addressed timeliness issues, including:

- Education provided to hospitals, midwives and birthing facilities to encourage earlier collection of newborn screening samples
- Expanded courier services
- Increased lab hours
- Improved lab processes and workflows
- Implementation of HIT systems to share data efficiently

An initiative for which HRSA provided funding that predated NewSTEPs 360 was a mini Collaborative Improvement and Innovation Network, (CoIIN), a type of learning collaborative. Eight newborn screening programs participated in the 18-month project. Representatives from states were paid to travel to APHL for in-person training, participated in webinars and received monthly coaching calls to improve performance on timeliness issues.

Following the success of the mini CoIIN, HRSA provided three years of funding for a newborn screening timeliness quality improvement initiative. Twenty-four states worked with NewSTEPs and NewSTEPs 360 staff, including in-person meetings, to address known challenges. Unlike the COIIN initiative, this project included funding that was given directly to the participating states, which allowed them to tackle individual challenges, such as:

- Education for hospital staff
- Sample collection and improved transit time to the labs
- Working on lab processes
- Working to improve how data are shared
- Getting results to providers faster

Dr. Sontag presented three videos produced by APHL and NewSTEPs. The first was from the mini CoIIN, where the eight participating states were asked to share their lessons learned. The video was recorded using smartphones. Top 10 Suggestions for Improving Newborn Screening Timeliness: https://www.youtube.com/watch?v=ei5t-D-RkZw&feature=youtu.be. The second was a video developed to show states how they could shoot a video with basic, inexpensive equipment, such as smartphones. In this video, families shared their stories about how newborn screening has impacted their lives: https://youtu.be/TrSh_kMf_zQ. In the final video, families thanked everyone working in newborn screening for their efforts to improve newborn screening: https://www.youtube.com/watch?v=taw9BBGklHU

Dr. Sontag also spotlighted a resource developed in partnership with the March of Dimes and the Association of State and Territorial Health Officials (ASTHO): a timeliness toolkit for states that helps them work towards expanded courier service and operating hours.

A. Discussion

- A Committee member asked about the original goal of the second video, whether it was intended to be disseminated through the programs. Dr. Sontag replied that the goal was twofold: to demonstrate how to develop a video and how to interview people in order to get the message out, which then helps with stakeholder buy-in. NewSTEPs is not tracking the number of times the video is viewed.

IV. Public Comments

The Committee had received no requests for public comments for the meeting, but Dr. Bocchini acknowledged a petition received on June 24th, 2018, supporting the addition of SMA to the RUSP, which had more than 2,000 signatures.

V. Education and Training Workgroup Update

Beth Tarini, M.D., M.S., FAAP
Committee Member
Chair, Education & Training Workgroup
University of Iowa Hospitals & Clinics

Dr. Tarini welcomed Dr. Cynthia Powell as the new Co-Chair of the Workgroup and thanked exiting Chair Cathy Wicklund, who rotated off the Committee, for her contributions to the Workgroup.

Next, she discussed the Workgroup's efforts on the communication guide, which is in the final stages of development. The Workgroup discussed obtaining feedback on the guide from pediatric and genetic residents and considering the option to link the guide to ACT sheets. The Workgroup also discussed the most effective way to distribute the guide to states. Ideas thus far include listservs used by people in state programs, APHL and the media.

The education guide, which points out elements of education in newborn screening and how they might map to stakeholder areas of interest, is also in its final development phase. The Workgroup is trying to identify a way to evaluate the guide and determine how best to track and monitor its usability and obtain feedback. In addition, the group is working to fine tune the introduction to target the end user by including more background and direction about the guide's utility.

Lastly, Dr. Tarini touched on two issues that arose in the Co-Chairs' meeting: provider and public education on newborn screening and the challenges inherent in communicating the limitations of newborn screening without detracting from its value. She mentioned that one target might be the North American Metabolic Academy as an avenue to reach specialists. We could learn from other communities that are doing screenings such as mammograms. She felt the best way to proceed would be to begin with a landscape assessment.

A. Discussion

- *AAP News* was suggested as a potential forum for sharing the document.
- Another Committee member agreed that we ought to look at what education resources are already available.
- It is important to educate clinicians who care for adult patients because some conditions identified in children have delayed onset.
- National board exams and residency training programs were suggested as other avenues for educating
- Linking the education material to opportunities to earn continuing education credits.
- It was noted that dissemination through the North American Metabolic Academy may not be effective because it reaches a very small number of people once a year and the curriculum is not easy to modify.
- A Committee member stated that geneticists are probably already aware that screening tests are not diagnostic tests.
- Dr. Berry offered to provide details about the MOC4 to ensure the Midwest Genetics Network efforts are made available, including a guide developed for a pediatric practice to distribute when conveying negative newborn screening results.

- An organizational representative said that evolving methodologies in education, such as the movement towards digital rather than printed materials, should be taken into account.

Dr. Bocchini suggested that the Education and Training Workgroup take the lead from this discussion and use the expertise of the laboratorians to gain specific information on test interpretation and other technical matters to allow those involved to work together to come up with clear guidance, definitions and interpretation.

VI. Laboratory Standards and Procedures Workgroup Update

Kellie Kelm, Ph.D.
Ex-Officio Committee Member
Chair Laboratory Standards and Procedures Workgroup
Food and Drug Administration

Dr. Kelm explained that she had discussed this workgroup's efforts in her earlier presentation but highlighted an article in *MMWR* on the effectiveness of screening for congenital hypothyroidism using one screen versus two screens, saying this might be a topic that would come around again.

A. Discussion

- A Committee member called attention to the potential increase in congenital hypothyroidism diagnoses and raised a few related issues: age-adjusted cut-offs, interpretation of diagnostic testing results, how to handle short-term follow-up. She suggested that this might offer an opportunity for cross-collaboration among the three workgroups. Another Committee member indicated cases ought to be followed for at least three years to determine whether they are true or transient cases.

Dr. Bocchini suggested putting together some presentations for the next meeting, which could help prepare the workgroups to consider and evaluate ideas to bring back to the full Committee.

VII. Follow-Up and Treatment Workgroup Update

Christopher Kus, M.D., MPH
Organization Representative
Co-Chair, Follow-Up and Treatment Workgroup
Association of State & Territorial Health Officials

Dr. Kus presented this update on behalf of Dr. Brosco. The Workgroup has completed its work on medical foods. The report will be sent to the HHS Secretary and posted on the Committee's website soon. The writing team also plans to submit a truncated version of the report for publication in a peer-reviewed journal. The quality measures report is also complete and will be posted on the Committee's website. The Workgroup plans to identify journals in which to publish the executive summary, consider topic-specific articles that build on the report and determine what aspects of the report tie into the roadmap project. The Workgroup is interested in other outreach ideas the Committee may have, to ensure the report gets to the people who can use the information.

The Workgroup is in the development phase of a long-term follow-up roadmap and will consider next steps based on Dr. Alex Kemper and K.K. Lam's Environmental Scan. Also in connection with the roadmap, Workgroup members Dr. Schneider and Dr. Ostrander offered some ideas for improving care by creating an integrated system for quality measures that the Workgroup discussed. Ideas include:

- Considering single registry and QI programs by disease or disease group
- Considering data consistency when evaluating follow-up for different conditions
- Devising a hub-and-spoke data collection system
- Patient identification and continuity
- Coordinated research/QI funding

Dr. Kus posed the following questions to the Committee:

- How can data registries inform quality measures to help improve informed treatment and follow-up?
- Is there interest in creating an integrated system for quality measures?
- Is there a need for a core set of data elements needed that is both disease specific and applicable across diseases?
- How can the Committee ensure newborn screening conditions have a follow-up plan?
- As new conditions are submitted for inclusion on the RUSP, should the submitter be required to include a follow-up plan relative to the condition?
- If a system was developed to report on newborn screening nationally, who would be responsible for it?

A. Discussion

- Dr. Ostrander said that that a follow-up and treatment plan should be an integral part of a proposal to add a condition to the RUSP. He noted, that this requirement might pose a barrier to adding new conditions to the RUSP. He also suggested establishing a standardized approach for establishing a follow-up data collection plan for conditions that are already on the RUSP. Dr. Ostrander also suggested the Committee could work toward encouraging centers to take responsibility as registry owners for their various diseases, to prevent inconsistencies caused by some registries being kept by disease groups and others by states.
- Dr. Bocchini found Dr. Ostrander’s comments to be relevant to the Committee’s plan to review the evidence review process thinking through what should be included when making decisions about what conditions ought to be recommend for the RUSP.
- The Newborn Screening Transitional Research Network’s work to create the Longitudinal Pediatric Data Resource, which devised a set of common data elements that are meant to be used across diseases, is a resource to consider. It was noted that how well the common data elements translate into clinical situations and how flexible they are needs to be considered.
- A Committee member stressed that long-term follow-up requires time, which equals money, and centers will not be able to do this without support. Who will provide the leadership for such a system and from where will the needed resources come.
- Dr. Kemper's and Dr. Lam's Environmental Scan, to be discussed in the next presentation, will be helpful in putting together a federated system.
- A Committee member suggested that planning for long-term follow-up should come before a disorder is proposed for addition to the RUSP and should be part of pilot studies.

VIII. Report on Long-Term Follow-Up in Newborn Screening

Alex Kemper M.D., M.P.H., M.S.
Division Chief of Ambulatory Pediatrics
Nationwide Children's Hospital
Professor of Pediatrics
Ohio State University College of Medicine

In his introduction, Dr. Bocchini pointed out that Drs. Kemper and Lam have been working with the Follow-Up and Treatment Workgroup due to the overlap in missions. Dr. Kemper discussed the work he and Dr. Lam have done on the "what is on the horizon" scan, which involved a landscape review to inform the Committee about opportunities for improving long-term follow-up. Long-term follow up has two different domains. One involves care and related special services and educational services that patients and families receive after a newborn screening diagnosis is made; the second is program evaluation, which involves quality improvements. He offered the Cystic Fibrosis Foundation as a model for capturing data for research due to its ability to certify clinics and collect data prospectively. He said that the Committee could consider the collection of prospective data in a more holistic way.

He broke down the four components of long-term follow up:

- Care coordination through a medical home
- Evidence-based treatment
- Continuous quality improvement
- New knowledge discovery

The enormous variations in the conditions, many of which have late-onset, make the study of these conditions challenging. Other challenges newborn screening programs face with regard to pursuing long term follow up include: the location and accessibility of experts, cost and fundamental knowledge about the condition, and the lack of ability to obtain authorization to collect data.

Dr. Kemper also touched on some of the work the Committee has already done on long-term follow-up, citing a 2011 publication that included what questions long-term follow-up should be able to answer and examining issues at the patient and family level, the medical-care and the medical-research level and at the state and national level. He noted that the Long-Term Follow-Up Workgroup identified barriers to tracking patients over time, including the need for standardized terminology for use in data sets, quality metrics, and information exchange, which touches on the federated system concept.

He highlighted several things included in the report, such as the fact that most newborn screening programs are conducting long-term follow-up. However, the extent and nature of the follow-up are variable.

The literature search produced a natural grouping of results. The first grouping focuses on recommendations about how to conduct long-term follow-up, such as the Committee's reports and other documents on data sharing for long-term follow-up. The second grouping focuses on prospective studies of data collected by newborn screening for the specific purpose of conducting long-term follow-up. The third was for prospective studies of the data collected outside of newborn screening programs for reasons other than long-term follow-up. The fourth grouping was retrospective studies of existing data collected for research or for non-research purposes, which would encompass any type of retrospective study.

He noted that retrospective studies provide a lot of important information and are feasible because the data are already there, although identifying the datasets and determining how to link them together pose challenges. The type of data you have will affect quality, for example, having access to claims data only rather than specific patient-level laboratory data. He added that registries that follow patients who are receiving specific therapy are helpful—such as Pompe disease registries—but gaining access to and ensuring a full understanding of what the registries contain can be difficult.

Dr. Kemper summarized the different types of studies. In prospective studies, a wide range of different conditions have been studied across multiple countries; the fact that they include a comparison population is an advantage. However, these studies are hard to conduct, often do not follow patients beyond six years and many studies focused on predictors of long-term outcomes based on initial presentation or on treatment. They often do not specifically address how success was achieved or the cost of collecting prospective data.

There are two types of retrospective studies: 1) chart audits, which can be helpful in learning about patients seen in one treatment center but there is no population against which to compare them; and 2) data linkage studies that can be more powerful in some ways because data from more subjects can be collected however there are also associated methodologic challenges. Retrospective studies are efficient for tracking rare disorders but it can take time for the outcomes to occur. Achieving linkage across the various datasets can be difficult.

Dr. Kemper then highlighted some examples of long-term follow-up activities, beginning with a web-based screening information system in California, which can support referral tracking and coordination, yielding a high-level accounting of patient information. A Colorado program includes a legislative requirement to report birth defects and other newborn disorders, which fosters dataset linkages. Illinois has an annual report based on data collected for children through 15 years of age. Minnesota has a dedicated long-term follow-up advisory team that is engaged in tracking outcomes and collection of parent-reported developmental status information on children. The NBS Connect program includes a patient registry and portal and focuses on inherited metabolic disorders.

Dr. Kemper summed up by stressing that it is important to use long-term follow-up to achieve care delivery and program evaluation and research. He indicated there are opportunities for retrospective studies to identify datasets and linkages, and to consider the risk of bias assessment. He urged the Committee to continue to think about what it can do to foster more complete long-term follow-up.

A. Discussion

- NORD has worked with patient advocacy groups to encourage patient-centered development of data collection for specific disorders. This could be a valuable resource, as some rare disease networks will crossover with newborn screening.
- The use of a single government identifier has come up several times through the years, but it generally has triggered public resistance.
- What type of resources would it take to collect these types of data? Could the Committee consider challenges?
- The Committee ought to consider redesigning the existing system to reap the maximum benefit. An examination of available resources could help, rather than trying to identify new funding sources for it.
- Although many natural history studies address long-term follow-up expenditures, some mechanisms have been developed to assist, including: 1) The Newborn Screening Translational

Research Network, a contract funded by ACMG, which is designed to capture datasets on many newborn screening conditions; 2) an algorithm that allows global identifiers to be generated and linked to a person without revealing any personally identifiable information; 3) the Rare Disease Clinical Research Network, which studies more than 100 rare diseases, half of which affect pediatric patients; and 4) A program announcement with specified review for natural history studies on conditions that either are or could beer part of newborn screening or that could be screened for a newborn.

- There is value to having historical controls in developing treatment trials for some conditions in newborn screening. Historical data has been instrumental in furthering FDA approval of an intervention or drug for a particular condition. However, the implementation of newborn screening changes the natural history of many of these conditions, which can be problematic when looking prospectively.
- Another Committee member pointed out that there is a lack of evidence-based treatment and management guidelines, saying that these are extremely important for quality improvement.
- A Committee member believes that the Committee does not have a good handle on how patient follow-up is being conducted in different places and asked Dr. Kemper whether the report will have more detail on this. Dr. Kemper said that the report will contain more detail and, when possible, will contain references to what the states are doing in this area, but will not include a survey of each state newborn screening program. NewSTEPs was suggested as a resource, including information on barriers to follow-up in states that currently do no follow cases long term.
- A Committee member said that it is also important to understand why states do long-term follow-up, noting that states' highest priority is whether affected individuals are receiving care, while providers are focusing on outcomes.
- Outcomes are a post-market surveillance problem The Orphan Drug Act addresses this by mandating data sharing once data shows a screen is indicated. This is to ensure that enough information is collected to come up with a long-term plan to improve care delivery.
- Dr. Brosco, as chair of the Long-Term Follow-Up Workgroup, said that the discussion has really helped to identify three activities that should be pursued: 1. Determine what type of follow-up to conduct for research purposes to show how to improve treatment; 2. Identify what needs to be done in terms of program evaluation to ensure that programs are well run; and 3. Determine what needs to be done at a population-health level to ensure that every child is receiving good treatment.

IX. Report on Technology in Newborn Screening

Alex R. Kemper, M.D., MPH, M.S.
Division Chief of Ambulatory Pediatrics
Nationwide Children's Hospital
Professor of Pediatrics
Ohio State University College of Medicine

Dr. Kemper and Dr. Lam have been developing a newborn screening technology compendium to provide high-level background information on screening methods, diagnostic approaches and treatment. With rapidly changing and nuanced technologies , it is important that everybody operate from the same place when talking about these activities.

A technical expert panel was convened, and, after looking at the literature, the panel identified areas that are helpful for everyone. As a result, a standard template (which Dr. Kemper displayed in his presentation) has been developed to describe a particular technology, its newborn screening application and, if it is a screening test, its accuracy. There is also a harms and risks section for each technology that covers potential unintended outcomes, false positives, cutoffs, resources needed, special considerations around regulatory issues, FDA approval and key references.

A. Discussion

- A Committee member said that it would be helpful to include the cost for a specific technology in the template rather than simply saying, "reduce the cost." Dr. Kemper replied that they will put in costs when they are known, although cost data are hard to come by.
- Another Committee member reminded the Committee that APHL and CDC provide week-long, hands-on training courses for various newborn screening technologies and offered to leverage that experience to provide relevant information.

X. New Business

Joseph Bocchini, M.D.
Committee Chair

No suggestions for new business were forthcoming.

XI. Adjourn

Dr. Bocchini thanked everyone for their participation, saying it is clear that a significant amount of effort is being made to move projects forward and to bring information to the Committee to inform its work. He announced that some members will be hearing from the Committee soon about serving on the Steering Committee or participating in the upcoming review of the nomination process, the evidence review process and the decision-making process.

The next meeting will be held at HRSA headquarters in Rockville on November 1-2, 2018.