Prioritization of Review for Conditions Nominated to the ACHDNC

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Project Goals

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1. Explore an alternative strategy for soliciting nominations
2. Develop an approach to prioritization when there is more than one condition at a time that meets the criteria for evidence-based review
3. Provide input to the ACHDNC about potential revisions to the nomination form and the decision matrix

The decision matrix will be discussed in the next presentation

Alternative Strategy for Condition Nomination

Current Nomination Process

- Advocates submit the nomination package, including information on:
  - The case definition of the condition
  - Natural history
  - Accuracy of screening
  - Benefits and harms of treatment
  - Outcomes of prospective newborn screening activities
- DFO confirms all material submitted
- The Committee's Nomination and Prioritization Workgroup reviews the package and might ask for additional information
- Workgroup and Chair present to the full committee in determining whether the condition should move to full evidence review

Challenges with the Current Nomination Process

- Requires significant work to nominate a condition, which could disadvantage advocates whose conditions are not well resourced
- Despite efforts to make the requirements for the nomination package clear, there can be important gaps

Alternative Approach to Condition Nomination

- Alternative approach could build on the US Preventive Services Task Force approach.
- Important to have advocates engaged in the process.

Alternative Approach to Condition Nomination

1. The ACHDNC website would allow for advocates to nominate a condition with basic information (e.g., case definition, screening method, contact information of the nominator)
2. The Nomination and Prioritization Workgroup would determine if nominations are sufficiently clear and in-scope.
3. For those that move forward, HHS/HRSA would develop the nomination package (internally or externally), with feedback from the nominators and subject matter experts.
4. The Nomination and Prioritization Workgroup would consider the package with a recommendation to the ACHDNC according to its usual process

Strategy for Prioritizing Nominated Topics

Rationale for Considering Prioritization

- Prepare for the possibility that multiple conditions could be eligible for referral to evidence-based review
- Prioritization is not to stop a condition that meets the criteria for referral for evidence-based review from moving forward
- Key consideration for prioritization – potential public health impact

Summary of Approach

- Point system modeled on the previous American College of Medical Genetics (now American College of Medical Genetics and Genomics) approach to the initial RUSP
- Caveats
  - Point system based on consensus
  - Not intended to capture all elements of screening for the targeted conditions
  - Based on what is available in the nomination package
  - Relies on values and opinions of each person assigning points
- Differences can be resolved by consensus
- The process will evolve over time with experience and further validation
- The point system is different than the ACHDNC recommendation process; it is only intended for prioritization

Category	Criterion	Description	Threshold	Points
A	Case Definition at the Time of Newborn Screening	The nomination package provides a clear case definition for establishing the presence of the nominated phenotype(s) presymptomatically	No	0.5
			Yes	1
B	Birth Prevalence	The expected birth prevalence of the nominated phenotype(s). If uncertainty, use the most reasonable category associated with the highest point value.	<1:500,000	0.2
			1:500,000 to 1:250,000	1
			1:250,000 to 1:100,000	2
			1:100,000 to 1:50,000	3
			>1:50,000	4
C	Natural History	Likelihood of poor outcome when treatment is initiated after clinical identification. Use your judgment to determine the threshold of likelihood and what is considered a poor outcome.	Moderate likelihood	1
			High likelihood	5
D	Outcomes from presymptomatic identification	Likelihood of improved quality of life or length of life when treatment is initiated prior to the development of significant signs or symptoms. Use your judgment to determine the threshold of likelihood and what is considered to be improved.	High likelihood	5
			Moderate Likelihood	2
			Low likelihood	0.5
E	Feasibility of Screening	The resources needed to implement screening for the nominated phenotype(s).	Requires new platform or approach, additional sample, or additional punch from the dried-blood spot	0.5
			Can be implemented into current newborn screening process	5
F	Diagnostic Uncertainty	The risk of identifying individuals with diagnostic uncertainty requiring follow-up for 3 or more months. Use	Low risk	1
			Medium or high risk	0.5

This approach prioritizes

- Conditions with a clear case definition
- Significant public health burden
- Pre-symptomatic treatment likely to be beneficial
- Secondarily, screening that could be implemented without a significant risk of diagnostic uncertainty

Final Score: $(A \cdot B \cdot C \cdot D) + (E \cdot F)$

Implementation

- Members of the Nomination and Prioritization Workgroup would individually assign points
- Differences resolved with discussion
- Final score and rationale presented to the ACHDNC

Lessons from Pilot Testing the Scoring System

Rank	Condition Nomination	Year Nominated	NPR Score (min, max)
1	Severe Combined Immunodeficiency	2007	69.3 (38, 105)
2	Pompe Disease	2012	55.5 (6, 105)
3	GAMT Deficiency	2021	55 (55, 55)
4	X-Linked Adrenoleukodystrophy	2013	54.2 (5.2, 105)
5	Spinal Muscular Atrophy	2017	53.5 (15, 45)
6	Mucopolysaccharidosis Type I	2012	30.5 (6, 55)
7	Critical Congenital Heart Disease	2009	20.5 (20.5, 20.5)
8	Mucopolysaccharidosis Type II	2021	14.4 (8.5, 32.5)
9	Krabbe Disease	2022	10.5 (8.5, 12.5)

- Does seem to distinguish conditions
- Sometimes wide variation in scoring, which could be related to the information available on the nomination form

Next Steps

Considerations for the ACHDNC

- Modification of the process used for the nomination process
  - One approach: Specific nomination period (e.g., January-August) with other periods for preparation of packages and ACHDNC consideration
  - Use of a scoring system when more than one nomination must be prioritized
- Update to ACHDNC processes based on these decisions, including update of the nomination form to better align with the point system and potentially updating the decision matrix

Questions