Topic Brief: Early Identification of Neuromuscular Disorders

Date: 12/2/2019
Nomination Number: 0888

Purpose: This document summarizes the information addressing a nomination submitted on October 17, 2019 through the Effective Health Care Website. This information was used to inform the Evidence-based Practice Center (EPC) Program decisions about whether to produce an evidence report on the topic, and if so, what type of evidence report would be most suitable.

Issue: Neuromuscular disorders, which are primarily of genetic etiology, have historically been untreatable. With the emergence of treatments, a review of evidence for the effectiveness of earlier screening for detection of motor delays/hypotonia that may underlie neuromuscular disorders was requested.

Program Decision:

The EPC Program will not develop a new systematic review because we did not find enough primary studies addressing the concerns of this nomination.

Key Findings

No studies on the effectiveness or harms of early screening for motor delays/hypotonia were identified.

Background

The American Academy of Pediatrics (AAP) recommends that children attend Well-Child visits to their pediatrician from ages 3 to 5 days to 21 years. Well-Child visits include tracking of the child's growth and development.[1] Current AAP guidelines recommend developmental screening, or formal assessment, at 9- 18-, and 30-month visits[2], in addition to ongoing developmental surveillance, or skilled observation by the physician and reported observations by the caregivers.[3]

Categories of development addressed in developmental screening and surveillance include gross and fine motor functioning.[2] Motor delays and hypotonia (decreased muscle tone) can indicate underlying neuromuscular disorders,[4] which include amyotrophic lateral sclerosis, multiple sclerosis, and muscular dystrophy. The prevalence of neuromuscular disorders, as determined in 2015, was between 1 and 10 per 100,000 people.[5] While neuromuscular disorders are primarily genetic and have historically been untreatable, treatments are now being developed.[6] Early detection and treatment of neuromuscular disorders could potentially lead to improved function.

Nomination Summary

Given the development of treatments for neuromuscular disorders, the nominators would like an assessment of evidence to determine the appropriateness of an extension of the current schedule of the AAP developmental screening, such that screening for motor delays and hypotonia begins at 2 months, as opposed to 9 months old.

Scope

1. Question 1: What is the effectiveness of early developmental screening for detection of motor delays/hypotonia, and neuromuscular disorders in children with no known motor delays?
2. Question 2: What are the harms of early developmental screening for motor delays/hypotonia in children with no known motor delays?

Table 1. Questions and PICOTS (population, intervention, comparator, outcome)

Questions	1. Effectiveness of early screening	2. Harms of early screening
Population	Children ages 0-4 years old	Children ages 0-4 years old
Interventions	Developmental screening for motor delays/hypotonia using a standardized test (e.g., Ages and Stages Questionnaires, Battelle Developmental Inventory Screening, Brigance Screens-II, Denver-11 Developmental Screening Test, Infant Development Inventory) starting at 2 months of age	Developmental screening for motor delays/hypotonia using a standardized test (e.g., Ages and Stages Questionnaires, Battelle Developmental Inventory Screening, Brigance Screens-II, Denver-11 Developmental Screening Test, Infant Development Inventory) starting at 2 months of age
Comparators	TAU (surveillance) starting at 2 months, followed by screening at 9 months and older, as recommended by Bright Futures	TAU (surveillance) starting at 2 months, followed by screening at 9 months and older, as recommended by Bright Futures
Outcomes	• Detection of motor delays, hypotonia, and neuromuscular disorders (e.g., multiple sclerosis, muscular dystrophy) • Function • Quality of life • Mortality	Harms (e.g., time burden to patient and family, and provider, false positives, resource utilization)

Assessment Methods

See Appendix A.

Summary of Literature Findings

We did not identify any systematic reviews or primary studies to address the key questions.

See Appendix B for detailed assessments of all EPC selection criteria.

Summary of Selection Criteria Assessment

We did not identify any systematic reviews or primary literature to assess the effectiveness or harms of early screening for motor delays/hypotonia.

Please see Appendix B for detailed assessments of individual EPC Program selection criteria.

Related Resources

We identified additional information in the course of our assessment that might be useful. We identified a review of motor function tests in children ages 0-2 years that was published in 2018.[7]

The study reviewed five screening tests that were validated in children from the general population. None of the identified tests indicated suitability for children as young as 2 months old, and two were potentially suitable for children 3 months old. This review was not considered duplicative as there was no evaluation of how these screening tools compared to the accuracy of surveillance alone.

References

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Appendix A: Methods

We assessed nomination for priority for a systematic review or other AHRQ Effective Health Care report with a hierarchical process using established selection criteria. Assessment of each criteria determined the need to evaluate the next one. See Appendix B for detailed description of the criteria.

Appropriateness and Importance

We assessed the nomination for appropriateness and importance.

Desirability of New Review/Absence of Duplication

We searched for high-quality, completed or in-process evidence reviews published in the last three years November 15, 2016 to November 15, 2019 on the questions of the nomination from these sources:

- AHRQ: Evidence reports and technology assessments
  - AHRQ Evidence Reports https://www.ahrq.gov/research/findings/evidence-based-reports/index.html
  - EHC Program https://effectivehealthcare.ahrq.gov/
  - US Preventive Services Task Force https://www.uspreventiveservicestaskforce.org/
  - AHRQ Technology Assessment Program https://www.ahrq.gov/research/findings/ta/index.html
- US Department of Veterans Affairs Products publications
  - Evidence Synthesis Program https://www.hsrd.research.va.gov/publications/esp/
  - VA/Department of Defense Evidence-Based Clinical Practice Guideline Program https://www.healthquality.va.gov/
- Cochrane Systematic Reviews https://www.cochranelibrary.com/
- PROSPERO Database (international prospective register of systematic reviews and protocols) http://www.crd.york.ac.uk/prospero/
- PubMed https://www.ncbi.nlm.nih.gov/pubmed/

Impact of a New Evidence Review

The impact of a new evidence review was qualitatively assessed by analyzing the current standard of care, the existence of potential knowledge gaps, and practice variation. We considered whether it was possible for this review to influence the current state of practice through various dissemination pathways (practice recommendation, clinical guidelines, etc.).

Feasibility of New Evidence Review

We conducted a limited literature search in PubMed from the last five years, November 26, 2014 to November 26, 2019, on parts of the nomination scope not addressed by earlier identified systematic reviews. We reviewed all identified titles and abstracts for inclusion and classified identified studies by question and study design to estimate the size and scope of a potential evidence review.

Search Strategy
Ovid MEDLINE(R)
Date searched: November 26, 2019

#	**Searches**	Results
1	exp Neuromuscular Diseases/ or Muscle Hypotonia/ or Motor Skills Disorders/ or exp Muscular Atrophy, Spinal/ or Muscular Disorders, Atrophic/ or exp Muscular Dystrophies/ or Multiple Sclerosis/	353191
2	(hypotonia or hypotonic or ((motor* or neuromotor or neuro-motor or neuromuscular or neuro-muscular) adj2 (disease* or disorder*)) or ((muscle* or muscular) adj2 (atroph* or dystroph*)) or "multiple sclerosis").ti,ab,kf.	148191
3	or/1-2	421383
4	Mass Screening/	100106
5	((standard* adj3 (assessment* or evaluat* or instrument* or questionnaire* or scale or scales or test or tests or testing)) or "Active and Passive Muscle Power" or "Ages and Stages" or Alberta or Amiel-Tison or Battelle or Bayley or Brigance or Denver or "Early Motor Questionnaire" or Hammersmith or Harris or "Infant Development Inventory" or "Infant Neurological International Battery" or INFANIB or "Movement Assessment of Infants" or "Neonatal Intensive Care Unit Network" or "Neuromotor Behavioral Inventory" or Peabody or Prechtl or "Primitive Reflex Profile" or "Standardized Infant NeuroDevelopmental" or "Structured Observation of Motor Performance" or "Test of Infant Motor Performance" or "Toddler and Infant Motor Evaluation" or Touwen or assessment* or Premie-Neuro).ti,ab,kf.	1096625
6	or/4-5	1186893
7	Developmental Disabilities/	19502
8	(((motor or neuromotor or neuro-motor or neuromuscular* or neuro-muscular*) adj3 (delay* or development* or function* or performance)) or (develop* adj3 (delay* or disabilit* or disorder*))).ti,ab,kf.	119080
9	or/7-8	130045
10	and/3,6,9	1763
11	limit 10 to ("all infant (birth to 23 months)" or "preschool child (2 to 5 years)")	651
12	10 and (infant* or toddler* or preschool* or (("1" or "2" or "3" or "4" or one or two or three or four or first or second or third or fourth) adj2 (month* or year*) adj2 (age or aged or ages or old)) or "well visit" or "well visits").ti,ab,kf.	391
13	or/11-12	714
14	limit 13 to english language	679
15	14 not ((exp animals/ not humans/) or (mice or mouse or rat or rats).ti.)	675
16	randomized controlled trials as topic/ or random allocation/ or double-blind method/ or single-blind method/ or exp clinical trial as topic/ or ("randomized controlled trial" or "controlled clinical trial" or "clinical trial").pt. or ((clin* adj5 trial*) or ((single* or doubl* or trebl* or tripl*) adj2 (blind* or mask*)) or control* or placebo* or random*).ti,ab.	4946066
17	and/15-16	224
18	limit 17 to yr="2015 -Current"	66
19	Observational Study/ or Comparative Study/ or Case-Control Studies/ or Cohort Studies/ or Follow-Up Studies/ or Longitudinal Studies/ or Prospective Studies/ or Retrospective Studies/ or Controlled Before-After Studies/ or Cross-Sectional Studies/ or Interrupted Time Series Analysis/ or ("comparative study" or "observational study").pt. or (observational or case-control or "case series" or cohort* or follow-up or longitudinal or prospective or retrospective or before-after or cross-sectional or "interrupted time series").ti,ab.	4966915
20	and/15,19	388
21	limit 20 to yr="2015 -Current"	110

#	Searches	Results
22	Cochrane database of systematic reviews.jn. or (meta-analysis or systematic review).pt. or (Medline or search or systematic review).tw.	459077
23	and/15,22	26
24	limit 23 to yr="2015 -Current"	16
25	17 or 20 or 23	493
26	15 not 25	182
27	limit 26 to yr="2015 -Current"	43

https://clinicaltrials.gov/ct2/results?show_xprt=Y&xprt=%28+screen+OR+standardized+AND+%28+assessment+OR+evaluation+OR+instrument+OR+questionnaire+OR+scale+OR+test+%29+OR+EXPAND%5BConcept%5D+%22Active+and+Passive+Muscle+Power%22+OR+EXPAND%5BConcept%5D+%22Ages+and+Stages%22+OR+Alberta+OR+Amiel-Tison+OR+Battelle+OR+Bayley+OR+Brigance+OR+Denver+OR+EXPAND%5BConcept%5D+%22Early+Motor+Questionnaire%22+OR+Hammersmith+OR+Harris+OR+EXPAND%5BConcept%5D+%22Infant+Development+Inventory%22+OR+EXPAND%5BConcept%5D+%22Infant+Neurological+International+Battery%22+OR+INFANIB+OR+EXPAND%5BConcept%5D+%22Movement+Assessment+of+Infants%22+OR+EXPAND%5BConcept%5D+%22Neonatal+Intensive+Care+Unit+Network%22+OR+EXPAND%5BConcept%5D+%22Neuromotor+Behavioral+Inventory%22+OR+Peabody+OR+Prechtl+OR+EXPAND%5BConcept%5D+%22Primitive+Reflex+Profile%22+OR+EXPAND%5BConcept%5D+%22Standardized+Infant+NeuroDevelopmental%22+OR+EXPAND%5BConcept%5D+%22Structured+Observation+of+Motor+Performance%22+OR+EXPAND%5BConcept%5D+%22Test+of+Infant+Motor+Performance%22+OR+EXPAND%5BConcept%5D+%22Toddler+and+Infant+Motor+Evaluation%22+OR+Touwen+OR+Premie-Neuro+%29+AND+%28infant+OR+toddler+OR+preschool+OR+%28%28month+OR+year%29+AND+%28age+or+aged+or+old%29%29%29+AND+AREA%5BConditionSearch%5D+%28+Neuromuscular+OR+neuro-muscular+OR+hypotonia+OR+motor+skills+disorder+OR+Muscular+Dystrophy+OR+Multiple+Sclerosis+OR+neuromotor+OR+neuro-motor+OR+muscular+atrophy+%29+AND+EXPAND%5BTerm%5D+%28+AREA%5BMinimumAge%5D+%28+MISSING+OR+RANGE%5BMIN%2C+4+years%5D+%29+AND+AREA%5BMaximumAge%5D+%28+MISSING+OR+RANGE%5B4+years%2C+MAX%5D+%29+%29

Appendix B. Selection Criteria Assessment

Selection Criteria	Assessment
1. Appropriateness	
1a. Does the nomination represent a health care drug, intervention, device, technology, or health care system/setting available (or soon to be available) in the U.S.?	Yes
1b. Is the nomination a request for an evidence report?	Yes
1c. Is the focus on effectiveness or comparative effectiveness?	Yes
1d. Is the nomination focus supported by a logic model or biologic plausibility? Is it consistent or coherent with what is known about the topic?	Yes
2. Importance	
2a. Represents a significant disease burden; large proportion of the population	Yes. The prevalence of neuromuscular disorders, as determined in 2015, was between 1 and 10 per 100,000 people.[5]
2b. Is of high public interest; affects health care decision making, outcomes, or costs for a large proportion of the US population or for a vulnerable population	Yes. The prevalence of neuromuscular disorders, as determined in 2015, was between 1 and 10 per 100,000 people.[5] Annual per-patient costs, as determined in 2014, were $63,693 for amyotrophic lateral sclerosis, $50,952 for Duchenne muscular dystrophy, and $32,236 million for myotonic dystrophy.[8]
2c. Incorporates issues around both clinical benefits and potential clinical harms	Yes.
2d. Represents high costs due to common use, high unit costs, or high associated costs to consumers, to patients, to health care systems, or to payers	Yes. Annual per-patient costs, as determined in 2014, were $63,693 for amyotrophic lateral sclerosis, $50,952 for Duchenne muscular dystrophy, and $32,236 million for myotonic dystrophy.[8]
3. Desirability of a New Evidence Review/Absence of Duplication	
3. A recent high-quality systematic review or other evidence review is not available on this topic	Yes.
4. Impact of a New Evidence Review	
4a. Is the standard of care unclear (guidelines not available or guidelines inconsistent, indicating an information gap that may be addressed by a new evidence review)?	No. Guidelines are available and a revision of the current AAP Bright Futures guidelines is currently underway.
4b. Is there practice variation (guideline inconsistent with current practice, indicating a potential implementation gap and not best addressed by a new evidence review)?	Yes. The development of treatments may warrant the evaluation of current screening, as it is possible that earlier screening could lead to early intervention.
5. Primary Research	
5. Effectively utilizes existing research and knowledge by considering: - Adequacy (type and volume) of research for conducting a systematic review - Newly available evidence (particularly for updates or new technologies)	We did not identify any primary studies that addressed the key questions.

Abbreviations: AHRQ=Agency for Healthcare Research and Quality