Research White Paper

Developmental Disabilities Issues Exploration Forum: Cerebral Palsy

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Preface

The Agency for Healthcare Research and Quality (AHRQ), through its Evidence-based Practice Centers (EPCs), sponsors the development of evidence reports and technology assessments to assist public- and private-sector organizations in their efforts to improve the quality of health care in the United States. The reports and assessments provide organizations with comprehensive, science-based information on common, costly medical conditions and new health care technologies. The EPCs systematically review the relevant scientific literature on topics assigned to them by AHRQ and conduct additional analyses when appropriate prior to developing their reports and assessments.

To improve the scientific rigor of these evidence reports, AHRQ supports empiric research by the EPCs to help understand or improve complex methodologic issues in systematic reviews. These methods research projects are intended to contribute to the research base and be used to improve the science of systematic reviews. They are not intended to be guidance to the EPC program, although may be considered by EPCs along with other scientific research when determining EPC program methods guidance.

AHRQ expects that the EPC evidence reports and technology assessments will inform individual health plans, providers, and purchasers; as well as the health care system as a whole by providing important information to help improve health care quality. The reports undergo peer review prior to their release as a final report.

We welcome comments on this Methods Research Project. They may be sent by mail to the Task Order Officer named below at: Agency for Healthcare Research and Quality, 540 Gaither Road, Rockville, MD 20850, or by e-mail to epc@ahrq.hhs.gov.

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Structured Abstract

Background/Purpose. The Effective Health Care Program undertook a stakeholder engagement forum to determine and prioritize topics for comparative effectiveness reviews related to the priority condition "developmental delays," of which cerebral palsy (CP) was chosen as a developmental delay in need of such an analysis.

Literature Search. A literature search for guidelines, consensus statements, systematic reviews, and meta-analyses uncovered 104 articles related to CP treatment and management. Examination of the articles revealed a limited secondary literature in most aspects of the care of patients with CP.

Meeting Materials. Forty-one stakeholders were contacted to participate in two teleconferences and one in-person meeting. The stakeholders represented patients, families, advocates, clinicians, policymakers, public and private payers, Federal agencies, researchers, and methodologists. Stakeholders used the literature results as well as their own backgrounds and knowledge to develop an initial 88 potential topics for comparative effectiveness research which were subsequently prioritized into 24 topic areas for future research.

Meeting Results. Stakeholders identified future research needs for comparative effectiveness reviews, primary research, as well as suggestions for research translation, dissemination, and general concepts. Proposed topics for comparative effectiveness reviews of treatments for patients with CP included screening for secondary and related conditions, rehabilitation treatments following surgical interventions, surgical interventions versus nonsurgical interventions for spasticity, surgical interventions for spasticity in particular subgroups of patients, feeding and nutritional interventions, and speech and language interventions.

Conclusions. The Issues Exploration Forum for CP successfully brought together stakeholders from disparate disciplines to formulate comparative effectiveness review questions for further research. The stakeholders expressed the need for primary research, improved translation, dissemination, and methodological standardization of research in addition to reviews.

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Background

Cerebral Palsy

Cerebral palsy (CP) is "a group of permanent disorders of the development of movement and posture, causing activity limitation, that are attributed to nonprogressive disturbances that occurred in the developing fetal or infant brain. The motor disorders of cerebral palsy are often accompanied by disturbances of sensation, perception, cognition, communication, and behavior, by epilepsy, and by secondary musculoskeletal problems."[1] Prevalence estimates in the United States over the past 20 years have been approximately 2 to 4 cases per 1000 children under the age of 18.[2-9] In addition, advances in supportive medical care have allowed approximately 90 percent of children with CP to survive into adulthood, resulting in an estimated 400,000 adults living with CP in the United States.[10-15]

Children and adults with CP suffer from a variety of conditions including spasticity, nutrition problems, intellectual disability and seizures. Spasticity affects an estimated 70 to 90 percent of children and adults with CP, leading to functional disability including problems with gait, gross and fine movements, and hip dysfunction.[10,16-20] Frequent gastro-esophageal reflux and difficulties with swallowing may result in nutritional deficiencies.[21-23] Intellectual disability varies with subtype of CP and level of impairment, and people with CP may also suffer learning disabilities, behavioral problems, and attention deficit hyperactivity disorder.[10,16,24,25] More than 25 percent of people with CP may have seizures as well, with the highest rate of seizures occurring in those with the greatest intellectual disability.[10,16,24,25] Finally, children and adults with CP are subject to social, mental, educational, vocational, and medical problems associated with growth, development, and aging. As therapies have developed to mitigate some of the problems associated with CP, the need for management into later life has increased.[15,26]

The variability of severity and affected areas in children and adults with CP mean that individuals with CP are likely to be engaged in a range of therapies intended to target specific deficits.

Comparative Effectiveness Research and the Evidence-Based Practice Centers

The Agency for Healthcare Research and Quality (AHRQ) is the lead Federal agency responsible for improving the quality, safety, efficiency, and effectiveness of health care for all Americans. As part of the U.S. Department of Health and Human Services, AHRQ works to fulfill its mission by conducting and supporting health services and comparative effectiveness research with networks of leading academic institutions across the United States and Canada. A primary mechanism for this work has been the Effective Health Care (EHC) Program authorized in the Medicare Prescription Drug Improvement and Modernization Act of 2003.

The EHC Program was established to conduct and support research with a focus on outcomes, comparative clinical effectiveness, and appropriateness of pharmaceuticals, devices, and health care services. The program focuses on 14 priority health conditions (Table 1) defined by the Secretary of the U.S. Department of Health and Human Services and the research is informed by the needs of Medicare, Medicaid and the State Children's Health Insurance Program.

Table 1. Fourteen EHC Program priority conditions

Arthritis and nontraumatic joint disorders (Muscle, bone, and joint conditions)
Cancer
Cardiovascular disease, including stroke and hypertension (Heart and blood vessel conditions)
Dementia, including Alzheimer's Disease (Brain and nerve conditions)
Depression and other mental health disorders (Mental health)
Developmental delays, attention-deficit hyperactivity disorder, and autism
Diabetes mellitus
Functional limitations and disability
Infectious diseases, including HIV/AIDS
Obesity
Peptic ulcer disease and dyspepsia (Digestive system conditions)
Pregnancy, including preterm birth (Pregnancy and childbirth)
Pulmonary disease/asthma (Breathing conditions)
Substance abuse (Alcohol and drug abuse)

Under the American Recovery and Reinvestment Act (ARRA) of 2009, $1.1 billion was directed toward comparative effectiveness research. AHRQ received $300 million to support evidence synthesis (e.g., systematic reviews), generation (e.g., conduct of comparative trials or through analysis of datasets), translation and dissemination (e.g., production of materials for clinicians and patients). Funds were used to support eight evidence-based practice centers (EPCs) in the development of particular topic-related expertise in a subset of the priority conditions; the Vanderbilt EPC was asked to do so in topics that fit within the rubric of developmental disabilities. Other ARRA funds that were directed to AHRQ were invested in expanding the nominations to the EHC Program and to engage stakeholders to assist AHRQ to better understand which research gaps needed new research. To support and expand AHRQ's research efforts in the area of developmental disabilities, the Agency piloted an Issues Exploration Forum (IEF). The IEF was an opportunity for a range of stakeholder participants to provide input to the EHC Program related to developmental disabilities and in particular to CP.

AHRQ, the Vanderbilt EPC, and the Stakeholder Engagement Team (SET) from the EHC Program's Scientific Resource Center (SRC) and Oregon Health Sciences University Center for Evidence-based Policy collaborated to achieve the following primary objective of the IEF: to help identify and prioritize comparative effectiveness research topics for the purpose of conducting systematic reviews (evidence synthesis) in the clinical condition area of CP, in accordance with AHRQ's mission, goals and objectives.

Methods

Identification of Evidence Gaps and Development of Research Questions

A literature search was conducted to identify existing systematic reviews, guidelines and meta-analyses with the goal of identifying important gaps in currently available guidance documents. The literature search was conducted as a supplement to the stakeholder process and to assist in determining whether stakeholder priorities aligned with gaps in the review literature.

We retrieved reviews and guidelines on CP, including spastic diplegia, quadriplegia, and hemiplegia; congenital diplegia, quadriplegia, and hemiplegia; static encephalopath; and choreoathetosis. Our search was executed on May 21, 2010, and was updated on October 15, 2010. Our initial search employed the PubMed interface database, and searched from 1999 to the present. In the updated search, we added search terms for issues identified by stakeholders during the first conference call, including psychotherapy, physical fitness, quality of life (QOL), pain, comorbidities, transitions, cultural diversity, followup studies, and technologies. Controlled vocabulary terms served as the foundation of our search in the PubMed database, complemented by additional keyword phrases to represent CP in the clinical literature. We also employed indexing terms when possible to exclude undesired publication types (e.g., news), items from non-peer-reviewed journals, and items published in languages other than English (for a full list of search terms, see Appendix B).

Once we identified reviews through the electronic database search, we examined abstracts of guidelines, consensus statements, and meta-analyses to extract data relevant to treatment and prevention of CP, although for the purpose of generating systematic review topics, we only focused on treatment data. For the development of the frameworks for the main treatment targets of CP (presented on October 6, 2010), we extracted data from the full text articles of systematic reviews identified in our search (see Appendix E, Table E-1, for the list of systematic reviews). We were able to extract limited data. This does not indicate that primary research pertaining to the treatment of CP has not been conducted, but that there is little literature that has been synthesized into reviews or guidelines.

Stakeholder Engagement

Recruitment and preparation. The SRC SET compiled an initial list of potential stakeholder organizations to participate in the Cerebral Palsy Issues Exploration Forum (CP IEF) beginning in June 2010. AHRQ program staff, Vanderbilt project staff, and the SET all contributed names to the list. These experts were approached to participate in the Forum and to suggest additional experts that could be invited to participate. Experts from all fields relevant to the care of individuals with CP were selected. In consultation with the AHRQ Task Order Officer, 10 of the 40 stakeholder seats were designated for representatives from Federal partner agencies related to CP, and the remainder of the seats represented broad stakeholder perspectives including:

- Advocacy
- Consumer/patient/family member
- Frontline clinician
- Methodologist
- Payer

- Researcher

When possible, stakeholders who could represent multiple perspectives were prioritized (clinician/family member or researcher/patient) over single perspective stakeholders. Additionally, stakeholders were sought who faced and could articulate decisional dilemmas in day to day life/work in order to inform areas of greatest need and to generate topic ideas for CP research. All participants met the criteria of having direct experience with decisional dilemmas of people living with CP or in providing information in the form of evidence-based research or care for those individuals. These criteria were essential to getting as many perspectives as possible in order to get a complete view of the information needs of decisionmakers.

As the forum's budget limited attendance to 40 participants, the team worked to prioritize the initial list of potential participants in accordance with agreed upon criteria for participation, and based on particular stakeholder perspectives deemed essential for a successful forum. As a result of prioritization efforts, a list of 40 individuals categorized by stakeholder type/perspective was created and the remainder was placed on a substitution list.

Compilation and prioritization of the stakeholder list was a collaborative effort between the SET, Vanderbilt, and AHRQ. AHRQ maintained final approval of the participant list. Once the EHC Program staff and leadership approved the finalized list, the SET used standard practices to recruit participants. SET staff began recruitment with telephone contact followed up with a written invitation via electronic mail. SET staff provided potential participants with a brief overview of the forum verbally or in writing and extended an invitation to participate. If identified stakeholders were unable or uninterested in attending, they were asked to provide a name of an appropriate substitute from within their organization or unique stakeholder perspective. The SET then submitted the substitute's name to the AHRQ Task Order Officer (TOO) for approval prior to extending an invitation. If the invited individual was unable to provide the name of a substitute, the AHRQ TOO or other staff was consulted for guidance on whom to invite next from the previously compiled substitution list. When all substitutes were exhausted, the AHRQ TOO, SET and/or Vanderbilt staff identified new potential participants to fulfill the missing stakeholder perspective. The SET recorded recruitment status of all stakeholder participants and provided the TOO and other team members with weekly updates.

Confirmed forum participants were offered an optional orientation to AHRQ and the EHC Program. The SET offered various dates and times over the course of 4 weeks prior to the start of the forum. Participants were encouraged to register for a session as soon as possible. Orientation sessions with fewer than two participants were canceled and participants were offered an individual orientation by SET staff via telephone. Individual sessions were also offered to participants who were unable to attend any of the scheduled group times or who were recruited subsequent to the start of the forum. A full list of stakeholders who participated is provided in Appendix A.

SET staff conducted orientations via a Web hosted PowerPoint presentation that outlined the history, goals and objectives of the AHRQ EHC Program. Additionally, participants were informed of the EHC Program research processes most relevant to the forum including topic generation, nomination, and selection processes. The orientation also included a brief discussion of the goals and objectives of the forum and their roles as participants. In addition, participants were informed of all public involvement opportunities with the EHC Program. Materials distributed at the orientation included the Federal Coordinating Council's definition of Comparative Effectiveness Research (CER), a brief definition of Patient, Intervention,

Comparators, Outcomes, Timing, and Setting (PICOTS) and a draft version of the EHC Program selection criteria for new research. All materials were preapproved by the AHRQ TOO and staff prior to distribution to participants.

Stakeholder committee: Review and prioritization of research questions. The IEF on Cerebral Palsy consisted of two Webex conference calls and a day-long, face-to-face meeting at the AHRQ Conference Center in Rockville, Maryland. In addition, participants were invited to participate in a temporary online discussion board through the AHRQ EPC Program extranet and to offer ideas for research via an AHRQ-sponsored Web forum. Each participant received log in information and instructions for posting comments to the online forum. Staff also accepted topics by email and phone and posted them on behalf of the participants to the online forum.

The first conference call on August 17, 2010 was attended by 25 stakeholders. It included an overview by the SRC of the IEF goals and format, and background CP as a chosen topic area. All stakeholders were invited to share their background and interest in participating in the forum. Participants were also asked to describe specific decisional dilemmas they face as patients and families affected by CP, clinicians treating patients with CP and researchers working in the field. The results were grouped into six themes and confirmed by participants:

1. The importance of assessing the effectiveness of existing and new technologies
2. Methodological limitations of CER and the implications of these (e.g., lack of long-term studies, exclusion of individuals with cognitive impairment)
3. Lack of standards of care and subsequent variation in treatment (including variables such as differences in treatment philosophy, geography, access to care, QOL, and the need for evidence-based treatments across the lifespan)
4. Transitions from childhood to adulthood and geriatric care; aging with CP
5. Translation/dissemination of research
6. Identifying the underlying cause(s) of CP

Following the initial call and in preparation for the second conference call on October 6thparticipants were asked to respond to the framework described below to assist in developing ideas for research. This framework was developed by the SET team in previous EHC Program work with nonclinical stakeholders, and adapted for the CP IEF. Stakeholders were asked to think about their decisional dilemmas around CP and to identify the following elements:

- Describe the issue or question in one or two sentences
- For whom this is an issue?
- The specific clinical, treatment issues that need to be addressed
- The specific support or systemic issues that need to be addressed
- The changes you would hope to see
- Whether there are issues of timing
- The settings or context that are important to this issue

Participants were asked to submit their ideas on the electronic forum or by email to begin to compile a list of important issues related to CP for consideration for research prioritization.

The second conference call was held on October 6, 2010 and was attended by 29 stakeholders. The Vanderbilt EPC team presented a background review of existing guidance for treating and managing CP in the form of clinical practice guidelines, consensus statements and meta-analyses. As the goal of the overall project was to identify potential systematic review

topics, the review of the literature focused on existing reviews to assess the degree to which primary literature had been synthesized in a manner helpful to clinicians and other stakeholders. The stakeholders provided comments on existing evidence, raised additional information and studies that should be included in the review, and provided their perspectives on the information needed to address their "real life" decision dilemmas. The themes that emerged from the discussion included:

- Methodological challenges, including the mismatch of available research methodologies for CP concerns (such as need for longitudinal, observational studies), and inadequacy of information
- QOL issues across the life span
- Interventions (feeding, eating problems, surgical interventions)
- Protocols for standards of care and translation of evidence
- Need for a common understanding and framework, definitions and outcome measures

Participants were encouraged to use the Web forum to nominate specific research topics related to CP which would be prioritized during the in-person meeting on October 26, 2010. A list of 88 potential research topics/ideas was generated from the first two meetings and the online forum.

Priority setting process. Upon arriving at the AHRQ offices in Rockville, MD for the in-person meeting, stakeholders were asked to rank the list of 88 potential topics within the CP literature. The topics were sorted into four broad thematic areas as follows: (1) health care delivery, (2) research methods, (3) treatments and interventions, and (4) QOL issues. Each participant was given 15 total votes which they could allocate across the list of 88 topics—with the caveat that no topic could be allotted more than 5 votes. Staff compiled the first round of voting results at the start of the in-person meeting.

Prior to the start of the meeting, stakeholders were divided into four small groups corresponding to the thematic topic areas listed above. Stakeholders were assigned to small groups to ensure that the greatest possible number of concepts was discussed and diverse perspectives were represented in each group. Small groups were provided a list with the initial prioritization for their thematic area and were instructed to: 1) clarify initial primary research and comparative effectiveness research topics (using PICOTS framework), 2) generate potential additional topics, and 3) recommend further prioritization. All four groups discussed, refined and in some cases, combined the existing list of topics. In addition, the groups generated new ideas for research topics based on their workgroup discussions. These were presented to the full group when it was reconvened and all participants had the opportunity to comment on the revised topics. After the forum, EPC, SET and AHRQ staff compiled a final list of 24 topic areas for future research prioritized and acknowledged by the full group. The list of 24 was posted to the online forum.

Results

Literature Scan

Search strategies and yield are provided in Appendix B. After adding a small number of hand-searched articles, we had a pool of 3,418 citations for this topic. We identified 104 relevant articles that consisted of guidelines, consensus statements, meta-analyses, and systematic reviews. We identified 2,602 primary literature citations, approximately 500 of which were added from our update and thus identified due to stakeholder input.

Practice Guidelines and Consensus Statements

The practice guidelines and consensus statements identified through the literature search are summarized in Appendix C, Table C-1. Practice guidelines & consensus statements. The table includes population focus, intervention types, and a summary of the author's recommendations. Fourteen guidelines and consensus statements are identified in the search:

- four guidelines and consensus statements on **pharmacological treatments for spasticity**;[27-30]
- one guideline and one consensus statement on rehabilitation, **physical therapy (PT), and occupational therapy (OT)**;[31,32]
- three guidelines and consensus statements on **surgical interventions for spasticity**;[33-35] and
- five guidelines and consensus statements on **interdisciplinary treatment of spasticity (pharmacology, surgery, and rehabilitation)**.[10,17,36-38]

The meta-analyses are summarized in Appendix C Table C-2. Meta-analyses—treatment of CP & other. The inclusion/exclusion criteria, search dates, and summaries of the findings are listed in this table. There are 14 meta-analyses identified in the search:

- six meta-analyses on **pharmacological treatments for spasticity**;[39-44]
- one meta-analysis on **surgical interventions for spasticity**;[45] and
- seven meta-analyses on **rehabilitation**.[46-52]

A quantitative summary of the numbers of practice guidelines, consensus statements, or meta-analyses available does not fully capture the complexities and nuances of this literature. However, some important trends are apparent in the charts of these numerical summaries (see Appendix D, slides 7-12). For example, there were no meta-analyses on hip disorders or feeding/nutrition. These two categories only had one practice guideline each. The two categories most commonly reviewed in guidelines or meta-analyses were spasticity and gait/PT. In addition to these summary tables and charts, many of the practice guidelines, consensus statements, and meta-analyses are included in the organizing frameworks that are discussed below.

Systematic Reviews

Graphs summarizing the topics on which systematic reviews in CP have been conducted can be found in Appendix E. Some important trends are apparent in the charts. A total of 76 systematic reviews were identified.[11,15,18-22,25,29,30,39-44,49,50,53-110] Spasticity and Gait/PT were the two categories with the greatest number of systematic reviews. While the largest part of the

systematic reviews on Spasticity addressed pharmacological treatments, the largest part for both Gait/PT and for Upper extremity/OT were rehabilitation therapies. In addition to the summary charts describing both the quantities and categories of these systematic reviews, the content of the reviews was analyzed within the context of the organizing frameworks that are discussed in Appendix E.

Meetings

Stakeholder Discussion One. Twenty-five stakeholders participated in the first teleconference call of the IEF. Stakeholders were asked to answer the following questions during their introductions: 1) why did you agree to participate in the forum, 2) what are the related dilemmas you face regarding CP, and 3) is there new or additional information that would help with these decision-related dilemmas?

Most stakeholders agreed to participate in this forum (question 1) because they wanted to see what new information is available and how knowledge in the field can be moved forward, and they wanted to advocate for standards of care and better services for individuals with CP. A few indicated they wanted the opportunity to connect with other experts in the field.

In response to questions 2 and 3, stakeholders presented decisional dilemmas and need for information on the following topics:

- Transitioning into adulthood
- Work/employment
- QOL, including navigating social systems
- A lack of a standard of care
- A lack of a means for determining the effectiveness of treatments
- Methodological limitations in evidence-based synthesis due to diverse patient population
- A need for large longitudinal studies
- Understanding health disparities and barriers to care
- Translation/dissemination of research
- Biomarkers and screening for causal pathways

Stakeholder Discussion Two. Twenty-nine stakeholders participated in the second conference call of the IEF. The Vanderbilt EPC presented information on the methods used for data collection, including search engines and keywords, and provided call participants with a summary of the evidence. The purpose of the literature search was to identify existing systematic reviews, guidelines/consensus statements, and meta-analyses only. The systematic reviews were summarized into clinical frameworks. Two searches were conducted, with the second search capturing key terms related to topics deemed important to stakeholders based on the discussion in the first conference call. Despite limited reviews on many of these important topics, a primary literature exists and may therefore warrant further exploration for potential systematic review topics.

The literature addressed a variety of therapies for CP, including pharmacological treatments for spasticity, rehabilitation therapies, and surgical interventions. Information from the systematic reviews was organized into clinical frameworks divided by treatment target, as outlined in the section of this paper regarding meeting materials.

In response to the presentation of the Vanderbilt's frameworks, the stakeholders had feedback/suggestions on the following:

- Need for evidence-based guidelines or management plans to guide primary and subspecialty care regarding comprehensive management of patients with CP
- Need for standardized measures for outcomes related to transitioning; research needed on lifespan issues, including QOL
- Need for meta-analytic and primary studies powered to address the heterogeneity of the patient population
- Lack of primary care, subspecialty, and other providers for adults with CP
- Inconsistency in research methodologies resulting in subsequent inadequacy of information
- Need for large longitudinal primary research to determine outcomes of almost all interventions used in current practice (surgical, feeding, eating, communication, pain, etc.)
- Need for a registry of patients with CP

In-person meeting. Thirty-two stakeholders participated in the in-person meeting in Rockville, MD. The meeting objectives were to 1) review, discuss, and generate potential topics for systematic review in the area of CP, 2) prioritize potential evidence synthesis topics in the area of CP, and 3) identify additional research and methodological issues and needs related to CP. Twenty-four topics were prioritized by stakeholders who participated in the IEF. In response to stakeholder feedback in advance of the meeting, more time was spent discussing additional research needs and methodological issues than generating topics for systematic review and prioritizing potential research synthesis topics. Multiple stakeholders noted throughout the day that, while systematic reviews could be helpful, the greater need in CP research currently is evidence generation rather than evidence synthesis. Stakeholders hypothesized that the lack of quality evidence generation thus far has been related to funding cycle constraints, the difficulties of assessing development over time, lack of integrated methods, and lack of standardized outcomes, among other problems.

Major points of discussion focused on how to perform useful research, potential sites to increase the capability to perform research, and ways to disseminate the research. Participants recognized CP as a lifelong condition that requires research over the lifespan. They further emphasized holistic frameworks, specifically the International Classification of Functioning, Disability and Health (ICF) or ICF for children and youth, in order to study the many facets of CP. Stakeholders encouraged AHRQ and other researchers to include consumers and families in future research design. Stakeholders recognized that care is delivered primarily in nonmedical settings, which may limit the applicability of clinic-based research. Furthermore, they promoted the adoption of standard outcomes in CP research. Participants desired a network of centers and/or a national registry to conduct clinical practice research that could circumvent some of the methodological challenges of CP research. They emphasized the need for translation of evidence to all interested parties (clinicians, patients, families, advocacy groups, educators, payers).

To fulfill the primary objective for the IEF, stakeholders identified potential topics that could benefit from systematic review, and by the end of the IEF activities, prioritized 24 potential topics for research. These included studies of mobility and mobility devices (wheelchairs, standers, etc.); feeding and nutrition interventions; communication and speech therapies; interventions related to care coordination; and QOL interventions, specifically comparing social, medical, and pharmacologic treatments that influence QOL. Other studies that might be useful included subgroup analysis of existing meta-analyses, a clinical or cost-effectiveness study of

surgical and pharmacological interventions, or technology assessments. (See Appendix F for full list of outcomes).

Another important outcome of the in-person meeting was the expansion of stakeholder engagement with the AHRQ EHC Program. Stakeholders uniformly declared that they were interested in becoming more involved in the program. Twenty-one of the 32 stakeholders offered to help AHRQ with future work in specific topic areas. Most volunteered to help further refine the 24 potential research topics.

Discussion

The primary goal of this process was to generate topics for systematic review related to CP. Ideally, these topics would be related to decisional dilemmas faced by clinicians, patients, families of patients and policy-makers in determining appropriate course of therapy and there would be an adequate literature base in which to conduct a review. Therefore, this process was piloted to combine a literature-based assessment of the need for comparative effectiveness research with insights from stakeholders. The IEF process achieved the goal of identifying systematic review topics, and also provided a forum for communication in and across communities; identified areas of primary research that were considered essential; and generated discussion on methodologic issues necessary to move the field of CP treatment and research forward. Even more robust results could likely be obtained by addressing process limitations. Resource constraints limited the number and scope of participants. Similarly, although the most productive part of the process was the in-person meeting, resources limited face-to-face interaction to a single meeting.

A particular success of this process was the ability to engage a broad range of stakeholders. Indeed, several stakeholders expressed their appreciation for an opportunity to engage in discourse with colleagues and other constituents with whom they rarely interacted, and certainly rarely saw in person. The ongoing process of multiple phone calls, an extranet and an in-person meeting created an opportunity for discussion to grow and evolve in a way that a one-time survey would not have.

Over the course of the conference calls and via the extranet, stakeholders were vocal and engaged. For example, they generally disagreed with an initial organization of materials based on the current state of the literature around target treatment areas. Nonetheless, the ability to identify differences between how the stakeholders viewed issues around clinical care and research, and the way that the current literature has conceptualized it, has potential to inform future comparative effectiveness research, and speaks to the questionable applicability of the current research base.

As noted in the methods section, a literature search was conducted to inform the conversation with the stakeholders, and to gauge consistency of the stakeholders' impressions of what types of evidence syntheses are currently available with what is actually in the literature. Based on the dearth of literature, it is likely that many of the clinical practices that are common for children with CP are not adequately supported by evidence. This is even truer for adults with CP. There are uncertainties in all of the treatment areas presented. Although there are clear guidelines for a few specific treatments that include ratings of the level of evidence associated with the recommendations (e.g., pharmacological treatment of spasticity), many treatments for CP do not have detailed evidence-based nor widely accepted guidelines. A common theme among the evidence-based guidelines and systematic reviews is the paucity of randomized controlled trials (RCTs).

At the IEF meetings the stakeholders reaffirmed and expanded on several key points that align with the literature. Regardless of the therapy being considered consistent themes included the lack of RCTs, the lack of trials with long term followup, the need for better clinical outcome measures, and the difficulty associated with transitions to adulthood.[10,28,34,50] The stakeholders pointed out that many of the evidence-based guidelines, systematic reviews, and consensus statements were published 5 to 10 years ago. The stakeholders' familiarity with the primary literature was an invaluable asset to the IEF process. However this highlights two problematic

possibilities. One possibility is that the pace of primary research may be slow in many segments of the field. A second possibility is that primary research exists but has not been adequately synthesized. The IEF stakeholders identified topics both for review and for primary research.

Final Prioritization of Topics

The results of this IEF are divided into categories according to desired output: systematic review, technical brief, primary research, information dissemination. A further category of general concepts arose from consistently repeated themes of the IEF.
Prioritized effectiveness and comparative effectiveness research questions.

Proposed topics for systematic reviews include the following:

- Screening and prevention:
  - The effectiveness of screening for secondary and related conditions in patients with CP including hip disorders, swallowing dysfunction, etc.
- Interventions and treatment, surgical:
  - The effectiveness of rehabilitation interventions following surgical interventions in patients with CP.
  - The effectiveness of tendon lengthening compared to other interventions such as botulinum toxin, serial casting, and other nonsurgical interventions for patients with CP.
  - The effectiveness of surgical interventions for spasticity in specific types of patients with CP (ambulatory versus nonambulatory, cognitive impairment versus typical intelligence, differing underlying pathologies, etc).
- Interventions and treatment, nonsurgical:
  - The effectiveness of feeding and nutritional interventions for children with CP (0 to 6 years old versus older children).
  - The effectiveness of speech and language interventions, including therapy and devices, on young children with CP.

Technical briefs are documents prepared for EPCs that provide a description of the state of the science on a particular topic for which there are limited published data to support conclusions (www.effectivehealthcare.ahrq.gov/index.cfm/news-and-announcements/newsletter/newsletter-december-18-2008/ehc-program-mission/). Proposed topics for Technical Briefs include the following:

- Community, ancillary, and social support services:
  - The effectiveness of supportive services and social supports for the management of CP. Are there any data comparing supportive services versus biomedical interventions (pharmacological, surgery, etc) with the outcome of QOL? What is the effectiveness of community services?
  - The effectiveness of community or other supports for parents of children with CP.
- Assessment tools:
  - The effectiveness of diagnostic tools for pain assessment in patients with CP.
  - The most reliable, valid, and patient-centered tools for assessment of QOL for specific types of patients with CP (different levels of gross motor function, patients requiring ventilator support, etc.).
- State of the science:
  - The state of the science in CP regarding robotics, stem cells, etc.

Prioritized research priorities. There were many areas that warranted more primary research. The IEF process highlighted the following areas as a priority for primary research:

- Best practices:
  - Best practices for bathing, toileting, dressing, and overall QOL for families and children.
  - Therapeutic strategies (pharmacologic and nonpharmacologic) to alleviate and/or prevent pain throughout all stages of life.
  - Tools to assess QOL following surgical interventions.
- Patient-centered research:
  - Analysis of the impact of the loss of services with transition to adulthood for children with CP. How does educational status, employment status, and other needs modify this impact?
  - Research on swallowing function and interventions to promote healthy swallowing and oral feeding in children with CP.
  - Research on the impact of increased prevention services for children with CP.
  - Epidemiologic research on aging and adulthood with CP, including sexuality, pregnancy, later-life health conditions, etc.
- Research methods:
  - Systematic research on successful models of transition to adult services.
  - National registry to cover lifespan issues and to capture data on comorbidities, use of services, and treatments over time.
  - Network of centers to implement quality improvement methodologies for preventive and chronic care of patients with CP (children and adults). Priority to those methodologies that relate to premature death and to patients who have multiple impairments.

General concepts and themes. General concepts that were important to the discussion among stakeholders included the use of the World Health Organization International Classification of Functioning, Disability, and Health (ICF).[111] Stakeholders felt that new interventions should be assessed according to ICF outcome paradigms. Stakeholders noted the need for research to cover the life span. Another limitation for research and clinical practice is the wide variation of CP nomenclature and definitions. It was suggested that the adoption of the international definition of CP would address this problem.[1,112,113] Other emphasized concepts were care delivery including cultural issues and effective care coordination. A desire to focus on the patient and on clinical and functional outcomes framed the discussions. Stakeholders also recognized the importance of functional outcome data for payers and caregivers. Possible outcomes identified included the Gross Motor Function Classification System,[114,115] Functional Mobility Scale,[116] Manual Ability Classification System,[117] and the soon-to-be-published Communication Functional Classification System.[118] Priority should be given to outcomes that are of value to patients with CP and their caregivers.

The translation of scientific research and dissemination to families, consumers, and clinicians was identified as a key process needing further implementation. Translational documents which stakeholders identified as needed included:

- care plans for children who require communication devices and other augmentative speech and language interventions

- a consensus statement on pain management in patients with CP
- summary document of interventions for patients with severe physical disability but typical cognition
- current treatment guidelines for surgical interventions (e.g., patient information handouts at point of care)
- care map following the ICF model and guiding clinical decisionmaking at the point of care. This should incorporate chronic care and preventive care, along with anticipatory guidance and lifespan considerations. Broad implementation of a care map could facilitate multi-center data collection especially if managed electronically.
- Organization of Developmental Disabilities Stakeholder engagement and participation in future AHRQ research activities.

Lessons learned and limitations. Many stakeholders expressed advocacy as one reason for their participation in the IEF, and noted that AHRQ should develop a strategy to operationalize if it is to be considered a core value/principle in the future. Current opportunities for stakeholder involvement can be found on the AHRQ EHC Program Web site (www.effectivehealthcare.ahrq.gov) and include the AHRQ community forum initiative, collaboration with AHRQ EPC Program and academic centers to nominate and refine topics for evidence synthesis and evidence generation activities, and current Department of Health and Human Sciences initiatives (Administration on Developmental Disabilities) in collaboration with Federal partners such as the Centers for Disease Control and Prevention, National Institutes of Health, and the Health Resources and Services Administration.

Conclusions. The IEF for the treatment of CP was able to achieve the objectives of identifying potential topics for systematic review, prioritizing these topics, and identifying additional research and methodological issues that affect this field.

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List of Acronyms/Abbreviations

AHRQ	Agency for Healthcare Research and Quality
ARRA	American Recovery and Reinvestment Act
CER	comparative effectiveness research or review
CP	cerebral palsy
EHC	Effective Health Care
EPC	evidence-based practice center
ICF	International Classification of Functioning, Disability, and Health
IEF	Issues Exploration Forum
OT	occupational therapy
PICOTS	patient, intervention, comparators, outcomes, timing, and setting
PT	physical therapy
QOL	quality of life
RCT	randomized controlled trial
SET	Stakeholder Engagement Team
SRC	Scientific Resource Center
TOO	task order officer

Appendix A. List of Stakeholders

Federal

Beth Ansel, Ph.D., CCC-SLP
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Appendix B. Literature Search and Retrieval Process

The state of the existing literature will help to identify which systematic reviews will be helpful to guide future research. Therefore, the purpose of our literature search was to identify existing systematic reviews, guidelines and meta-analyses only. Therapeutic areas, research foci and outcomes not identified in our search, but considered important by stakeholders may be priorities for future systematic reviews.

Controlled vocabulary terms served as the foundation of our search in the PubMed database, complemented by additional keyword phrases to represent CP in the clinical literature. We also employed indexing terms when possible to exclude undesired publication types (e.g., news), items from non—peer-reviewed journals, and items published in languages other than English. We searched PubMed from 1999 forward and employed search strategies to retrieve reviews and guidelines on cerebral palsy, including spastic diplegia, quadriplegia, and hemiplegia; congenital diplegia, quadriplegia, and hemiplegia; static encephalopathy; and choreoathetosis. After input from the stakeholder identified additional areas of particular interest, we conducted a second search and added additional documents. Our second search included search strategies regarding issues deemed important by stakeholders, such as psychotherapy, physical fitness, quality of life, pain, comorbidities, transitions, cultural diversity, follow-up studies, and technologies.

Search Terms and Article Selection

Our search was executed on May 21, 2010, and was updated on October 15, 2010. Below (Tables B-1 and B-2) are our search terms and the yield from the PubMed database for both dates. After adding a small number of hand-searched articles, we had a pool of 3,418 citations for this topic. Since we are not conducting a full review at this time, and therefore not reviewing original research, we identified 151 relevant articles that consisted of guidelines, consensus statements, meta-analyses, and systematic reviews. We identified 2,602 primary literature citations, 527 of which were added from our second search. The reviews included in our search are summarized below. Importantly, a lack of information on topics of interest to the stakeholders was noted, particularly in areas such as:

- psychosocial effects of CP
- support for transitions
- psychotherapy
- physical fitness
- quality of life
- pain
- comorbidities
- transitions
- cultural diversity
- follow-up studies
- technologies

We note that despite the absence of reviews in this area, a primary literature does exist and may therefore warrant further exploration for potential systematic review topics.

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Cerebral palsy environmental scan search results: Last updated May 21, 2010

Table B-1. PubMed search strategies May

Search terms		Search results
#1	cerebral palsy[mh] OR cerebral palsy[tiab] OR cerebral palsies[tiab] OR spastic diplegia*[tiab] OR congenital diplegia*[tiab] OR static encephalopath*[tiab] OR congenital quadriplegia*[tiab] OR spastic quadriplegia*[tiab] OR spastic hemiplegia*[tiab] OR congenital hemiplegia*[tiab] OR choreoathetosis[tiab]	16,832
#2	therapy[sh] OR therapeutics[mh] OR teaching[mh] OR psychotherapy[mh] OR treatment outcome[mh] OR therap*[tiab] OR treatment*[tiab]	6,852,165
#3	#1 AND #2 AND eng[la] AND humans[mh] and 2000:2010[dp]	3,349
#4	#3 AND consensus development conference[pt]	5
#5	#3 AND letter[pt]	136
#6	#3 AND comment[pt]	160
#7	#3 AND case reports[pt]	387
#8	#3 AND review[pt]	668
#9	#3 AND practice guideline[pt]	6
#10	#3 AND news[pt]	5
#11	#3 AND editorial[pt]	56
#12	#3 AND historical article[pt]	14
#13	#3 AND meta-analysis[pt]	40
#14	#3 AND legal cases[pt]	2
#15	#3 NOT (#4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14)	2,076**

Key: [mh] Medical Subject Heading; [la] language; [tiab] title/abstract word; [pt] publication type; [sh] subheading
* wildcard symbol to allow searching for pluralizations
**Note: numbers do not tally as some articles are excluded in more than one category

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Cerebral palsy environmental scan search results Last updated October 15, 2010

Table B-2. PubMed search strategies October

Search terms		Search results
#1	cerebral palsy[mh] OR cerebral palsy[tiab] OR cerebral palsies[tiab] OR spastic diplegia*[tiab] OR congenital diplegia*[tiab] OR static encephalopath*[tiab] OR congenital quadriplegia*[tiab] OR spastic quadriplegia*[tiab] OR spastic hemiplegia*[tiab] OR congenital hemiplegia*[tiab] OR choreoathetosis[tiab]	17,229
#2	therapy[sh] OR therapeutics[mh] OR teaching[mh] OR psychotherapy[mh] OR treatment outcome[mh] OR therap*[tiab] OR treatment*[tiab] OR physical fitness[mh] OR exercise therapy[mh] OR physical therapy[mh] OR exercise[mh] OR fitness[tiab] OR exercise[tiab] OR quality of life[mh] OR quality of life[tiab] OR qol[tiab] OR analgesics[mh] OR pain[mh] OR pain[tiab] OR pain clinics[mh] OR analgesia[mh] OR comorbidity[mh] OR comorbidity[tiab] OR comorbid[tiab] OR comorbidities[tiab] OR transition[tiab] OR transitional[tiab] OR transitioning[tiab] OR adulthood[tiab] OR adolescent health services[mh] OR cultural diversity[mh] OR religion and medicine[mh] OR religion[mh] OR culture[mh] OR culture[tiab] OR cultural[tiab] OR long term[tiab] OR follow-up studies[mh] OR chronic disease[mh] OR technology[tiab] OR technologies[tiab] OR self-help devices[mh] OR educational technology[mh] OR technology[mh]	8,252,660
#3	#1 AND #2 AND eng[la] AND humans[mh] and 2000:2010[dp]	4,055
#4	#3 AND consensus development conference[pt]	5
#5	#3 AND letter[pt]	151
#6	#3 AND comment[pt]	184
#7	#3 AND case reports[pt]	438
#8	#3 AND review[pt]	764
#9	#3 AND practice guideline[pt]	7
#10	#3 AND news[pt]	5
#11	#3 AND editorial[pt]	67
#12	#3 AND historical article[pt]	17
#13	#3 AND meta-analysis[pt]	44
#14	#3 AND legal cases[pt]	2
	Search terms	**Search results**
#15	#3 AND addresses[pt]	3
#16	#3 AND bibliography[pt]	1
#17	#3 AND clinical conference[pt]	4
#18	#3 AND congresses[pt]	6
#19	#3 AND in vitro[pt]	3
#20	#3 AND interactive tutorial[pt]	2
#21	#3 AND lectures[pt]	3
#22	#3 NOT (#4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21)	2,590**

Key: [mh] Medical Subject Heading; [la] language; [tiab] title/abstract word; [pt] publication type; [sh] subheading;
* wildcard symbol to allow searching for pluralizations
**Note: numbers do not tally as some articles are excluded in more than one category

Appendix C. Existing Guidelines, Consensus Statements, and Meta-Analyses

From an electronic database literature search, we retrieved guidelines, consensus statements, and meta-analyses for the treatment and prevention of cerebral palsy. We identified 14 guidelines and consensus statements,[1-14] 13 meta-analyses regarding treatment of CP,[15-26,27] and 24 meta-analyses regarding prevention of CP.[28-51] Details from these reviews are provided below in Tables C1 and C2.

Four guidelines and consensus statements specifically address pharmacological treatments for spasticity, with publications from the American Academy of Neurology with the Child Neurology Society, Gillette Children's Specialty Healthcare, Arkansas Children's Hospital, and University of Florida.[2,7,11,12] These guidelines report that botulinum toxin type A (BoNT-A) is effective in upper and lower extremities; there is insufficient data on alcohol or BoNT-B injections, while two guidelines conflict in their assessment of the efficacy of phenol (Goldstein, et al indicate that phenol is an appropriate treatment option, whereas Delgado, et al., reports that there is insufficient data for use of phenol).[7,8,11,14] Diazepam and tizanidine are effective in the short-term for generalized spasticity, although one study warns that benzodiazepines may cause physiologic addiction and tolerance and require an increased dose.[7,12] Furthermore, there is insufficient data on dantrolene and oral baclofen, although studies differ on the use of intrathecal baclofen, with one study citing insufficient data on intrathecal baclofen, and another recommending its use as the treatment of choice for spastic tetraparesis.[7,9] Levodopa can be useful in spastic quadriplegia or mixed athetoid or spastic forms of CP. Notably, there is little data regarding functional outcomes and side effects for any of the pharmacologic treatments.

One guideline and one consensus statement specifically address rehabilitation therapies, physical therapy, physiotherapy, and occupational therapy. These guidelines and statements were composed by a Mac Keith Multidisciplinary Meeting and the Italian Society of Physical & Rehabilitation Medicine with the Italian Society of Child and Adolescent Neuropsychiatry.[4,5] The Mac Keith consensus statement focuses on postural therapy and the timing of postural therapy, as well as on monitoring hips for subluxation.[4] The Italian guidelines recommend consideration of therapies based on the characteristics of the subject.[5] Three guidelines and consensus statements focus on spasticity and surgical interventions, with two publications from University of Florida and another from the Semmes-Murphy Clinic.[1,9,10] These papers recommend that surgery be completed early in life if possible (4-7 years), that tendon-lengthening be used to manage some severe spasticity and soft-tissue complications, and that tendon transfer be used sparingly and only by well-trained surgeons.[1,10] According to these authors, several of the orthopedic interventions have unknown long-term effects, including selective dorsal rhizotomy (SDR), tendon release, and intrathecal baclofen, leading to a need for better outcome tools for measuring long-term success.[1] Four guidelines and consensus statements address spasticity from a holistic perspective, discussing aspects of pharmacology, surgery, rehabilitation, etc. These papers come from the Committee on Children with Disabilities, Washington University School of Medicine with the St. Louis Children's Hospital, Child Neurology Associates of the Scottish Rite Children's Medical Center, and the University of Florida.[6,8,13,14] The four guidelines and consensus statements recommend ongoing care in the medical home; using the Gross Motor Function Classification System (GMFCS) as a tool for severity classification and prognostication; maximizing nutrition; focusing on communication

and education, mobility, physical fitness, and independence as key factors for the CP patient; tailoring interventions to the patient; and recommending against use of electrical stimulation.

Six meta-analyses explore the utility of pharmacological therapies for treatment of spasticity in CP.[15,17-21] Their evidence supports use of BoNT-A as an adjunct for upper limb spasticity with occupational therapy,[15,17] and is also effective in the lower limb, especially for equinus foot.[18,19,21] There is insufficient evidence to support or refute use of specific therapy interventions after BoNT-A injections.[20] Another meta-analysis synthesizes the data on the use of surgical therapies for treatment of spasticity in CP, focusing on SDR, with a small but statistically significant improvement in SDR plus physical therapy in comparison to physical therapy alone for selected patients.[25] Seven meta-analyses present results of studies specifically focused on a variety of rehabilitation techniques for patients with CP.[16,22-24,26,27,52] These papers shows that muscle strengthening exercises are not effective for children and adolescents with CP who are able to walk,[16] and that many studies of interventions such as orthoses are difficult to synthesize due to the lack of standardized intervention techniques or outcomes.[24,27] Constraint-induced movement therapy (CIMT) is considered experimental but very promising

Table C-1. Practice guidelines & consensus statements

Reference	Year	Organization	Population Focus	Intervention(s)	Summary
Delgado et al.[7]	2010	Quality Standards Subcommittee of the American Academy of Neurology Practice Committee of the Child Neurology Society	children with CP	pharmacologic treatments for spasticity: botulinum toxin type A (BoNT-A), phenol, alcohol, botulinum B, diazepam, tizanidine, dantrolene, oral baclofen, and intrathecal baclofen)	localized/segmental spasticity: BoNT-A is effective in upper and lower extremities, conflicting evidence regarding functional outcomes; FDA is investigating isolated cases with poor outcomes insufficient data on phenol, alcohol, or botulinum toxin type B injections in localized/segmental spasticity generalized spasticity: diazepam effective (short-term), but insufficient data on effect on motor function outcomes and side effects; tizanidine effective, but insufficient data on effect on function and side effects; insufficient data on dantrolene, oral baclofen, and intrathecal baclofen
Gericke[4]	2006	Mac Keith	children with CP	individually-tailored postural management program may include special seating, night-time support, standing supports, active exercise, orthotics, surgical interventions, and individual therapy sessions	postural management programs in lying should begin as soon as appropriate after birth for children in Gross Motor Function Classification System (GMFCS) IV-V; sitting programs should begin at 6 months, standing programs at 12 months. postural management programs for children at GMFCS level III should emphasize postural activity form an early age children who cannot walk >10 steps by age 30 months should have hip x-ray to evaluate migration percentage of each hip, and x-ray should be repeated every 6-12 months until 7 years old or when further deformity is unlikely if hip migration percentage is greater than 14% at 30 months, postural management at night and ongoing radiological monitoring recommended children with GMFCS IV and V who are unable to stand until 5 years old should have spine x-rays at 5 and 10 years need for more evidence for effectiveness, achieved by establishing a uniform vocabulary used for postural/positional deformity and each center contributing a central database of children in need

Table C-1. Practice guidelines & consensus statements (continued)

Reference	Year	Organization	Population Focus	Intervention(s)	Summary
Ferrari & Cioni[5]	2004	Italian Society of Physical & Rehabilitation Medicine (SIMFER) Italian Society of Child & Adolescence Neuropsychiatry (SINPIA)	children with CP	guidelines for re-education for which the goal is to develop and improve adaptive functions	guidelines based on type of subject (motricity, lesion history, rehab history, complexity, complications, family, community), description of justified age related fields of intervention, and methodology international definition of CP is inadequate because it ignores some determinant components like sensory and perception deficits, distortions of mental representation, praxis and gnosis problems, and cognitive difficulties medical care proposals available for therapy are inhomogeneous if not contradictory guidelines for care and education of child must be drafted
Cooley [6]	2004	Committee on Children with Disabilities	children with CP	managing spasticity (physical therapy, orthopedic and orthotic management, and systemically or regionally administered medication) associated care (nutrition, dental, and pain management)	guidelines on ongoing care in the medical home; supporting children, youth, & families; and outcomes & quality of life GMFCS can provide a valid tool for severity classification of CP and prognostication of motor skills from a young age selective dorsal rhizotomy shows greatest benefit in young children (3-7 years old) with spastic diplegia but stable trunk control and good lower extremity strength nearly half of all children with CP have evidence of significant undernutrition includes pointers for pediatricians

Table C-1. Practice guidelines & consensus statements (continued)

Reference	Year	Organization	Population Focus	Intervention(s)	Summary
Brunstrom[8]	2001	Washington University School of Medicine St. Louis Children's Hospital	children with CP	multiple physical therapy, orthopedic, surgical, and medical interventions environmental manipulations: reducing sleep deprivation, alleviating pain, therapeutic use of heat and/or deep tissue massage, and reducing prolonged periods of immobility oral medications to treat dystonia: levodopa neurosurgical interventions: baclofen pump and selective dorsal rhizotomy	presents an approach to treatment of CP focusing on communication and education, mobility [assisted mobility, biomechanics, tone management, strength, and balance], physical fitness, and independence more research should be done on the effect of exercise on symptom improvement (alleviation of pain, increase of energy) standing and weight-bearing exercise promote normal bone development; stretching helps maintain and improve muscle-tendon length and joint range-of-motion (ROM); orthotics and bracing can improve gait and prevent muscle contractures and limb deformity; serial casting and botulinum toxin injection can improve ROM at contracted joints; orthopedic surgery can also be useful. Tailor interventions to situation. levodopa useful in spastic quadriplegia or mixed athetoid/spastic forms of CP regular aerobic exercise improves strength, physical fitness, and motor function home programs of stretching, strengthening, weight-bearing, and balance are needed; occupational therapy/physical therapy used as adjuncts to home therapy neuromuscular electrical stimulation and isokinetic strength training are promising new modalities

Table C-1. Practice guidelines & consensus statements (continued)

Reference	Year	Organization	Population Focus	Intervention(s)	Summary
Goldstein[14]	2001	Child Neurology Associates (Scottish Rite Children's Medical Center)	children with spasticity	rehabilitative therapies: physical and occupational therapy (limited evidence-based support for efficacy), adaptive equipment, and orthoses oral pharmacotherapy: baclofen, diazepam, tizanidine, dantrolene chemical denervation: phenol injections, botulinum toxin injections orthopedic surgery: SDR; intrathecal baclofen pump	rehabilitative therapies maximize patient function and optimize results of other medical and surgical interventions oral meds can be helpful in selected patients when a generalized reduction in body tone is desired, but there are adverse effects associated with use phenol is inexpensive in comparison to BoNT-A and is reported to exceed 12 months in duration of action, so is an appropriate treatment option in selected patients with focal spasticity risks associated with orthopedic interventions are small; they provide patients with immediate, long-lasting improvements in limb function SDR has sustained increasing popularity over the past two decades; despite the fact that it is limited to lumbosacral sensory rootlets, some patients sustain improvements in upper extremity tone as well candidates for intrathecal baclofen are those with severe, generalized spasticity that impedes independent function or ability of caregivers to assist; intrathecal baclofen reduces tone, improves range of motion, decreases painful muscle spasm, and improves measures of independent function, while reducing the need for subsequent orthopedic interventions recommendations for patient selection for spasticity management
Hesel[13]	2001	Shands Hospital, University of Florida	Children with spasticity	occupational therapy, physical therapy, speech therapy, orthotics	recommendations for the optimal use of each intervention based on age and/or diagnosis of patient
Krach[12]	2001	Gillette Children's Specialty Healthcare	children with spasticity	benzodiazepines (diazepam most commonly used for spasticity) baclofen dantrolene sodium alpha$_2$-adrenergic agonists gabapentin	treatment of spasticity in children has not been well documented (medications and outcomes) presence of spasticity alone is not considered sufficient to warrant its treatment benzodiazepines cause a physiologic addiction and tolerance resulting in increased dose most studies of oral baclofen have involved adults with spinal cord injury or multiple sclerosis

Table C-1. Practice guidelines & consensus statements (continued)

Reference	Year	Organization	Population Focus	Intervention(s)	Summary
Edgar[11]	2001	Arkansas Children's Hospital	cerebral palsy	botulinum toxin	toxin's goal is the complete or partial paralysis of specific target (agonist) muscles affecting a specific spastic joint while leaving the antagonist muscle unaffected, creating balance electromyography, kinetic joint analysis, determination of muscle lengthening, assessment of muscle strength, functional impairment measures such as the Ashworth Scale, and dexterity assessment determine the efficacy of BoNT-A both safe and well tolerated patient selection and evaluation are critical to BoNT-A success.
Woo[10]	2001	University of Florida	spastic cerebral palsy	orthopedic surgery (tendon lengthening, tendon transfer, osteotomy, and arthrodesis) physiotherapy orthoses serial casts	orthopedic surgery treats the secondary effects of the neurologic lesion as expressed in the bone and tissues, not to address the primary loss of neural cell function surgery should be completed between 4-7 years so as to avoid multiple surgeries tendon lengthening preferred method of managing soft-tissue complications of spasticity tendon transfer prone to poor outcomes there is no consensus regarding physiotherapy, so better outcome measurement tools and long-term follow-up studies need to be conducted serial casts stretch muscles when there is a mild deformity; orthoses are used for gait disorders

Table C-1. Practice guidelines & consensus statements (continued)

Reference	Year	Organization	Population Focus	Intervention(s)	Summary
Boop[1]	2001	Semmes-Murphy Clinic	spasticity	surgical interventions	social factors may be contraindications for certain interventions not necessary for child with severe spasticity to have failed oral antispasticity medication trials before being considered surgical candidate decision for surgical intervention should be based on severity of spasticity, effect on patient, and patient's size no prospective RCTs comparing long-term benefits of SDR to orthopedic tendon release or intrathecal baclofen the majority of children with severe spasticity may be optimally managed by treatment of underlying spasticity combined with serial casting or tendon release unknown long-term effects of replacement laminoplasty after multilevel laminectomy as part of SDR patients with pure hemiplegic CP are better treated with a combination of intrathecal baclofen and orthopedic interventions rather than SDR better outcome tools need to be developed for measuring success in patients undergoing surgical intervention for movement disorders related to CP; should incorporate quality of life measures a number of questions remain unanswered regarding the outcome of surgical interventions in CP; many could be answered by controlled prospective trials intrathecal baclofen and orthopedic interventions are treatment of choice for hemiplegic CP
Boop et al.[9]	2001	University of Florida	children with CP	SDR intrathecal baclofen therapy electrical stimulation selective peripheral neurotomy	not sure of the efficacy of SDR for children without ambulatory potential intrathecal baclofen is the treatment of choice for patients with spastic tetraparesis electrical stimulation has not gained acceptance research on new and improved pumps should be supported
Graveline et a[3]	2001	University of Florida	children with spasticity	consensus on physical management approaches	early referrals, communication among caregivers, continuity of care, comprehensive approach, seek evidence, consider life-long goals, apply existing outcome measures when possible for assessment

Table C-1. Practice guidelines & consensus statements (continued)

Reference	Year	Organization	Population Focus	Intervention(s)	Summary
Tilton and Maria[2]	2001	University of Florida	children with spasticity	pharmacotherapy: oral (baclofen, tizanidine, and benzodiazepine) & botulinum toxin	essential elements of a comprehensive approach to treatment include a) recognition that there are multiple treatment modalities available b) an initial multidisciplinary evaluation of the patient with regular re-evaluations to meet the changing needs of the patient c) individualized treatment plan d) plan with concise, explicit, short- and long-term goals embraced by patient, family, and health care providers factors affecting choice of therapeutic modality: focal or generalized spasticity, comorbidities, cost, age, dosing, compliance adherence, side effects, prior reaction, past options

Table C-2. Meta-analyses—treatment of CP & other

Reference	Year	Inclusion/Exclusion Criteria	Search Dates	Summary of treatment or other
Arpino et al.[52]	2010	All RCTs published in English, using extended terms for CP and rehabilitation/physical therapy/neurodevelopmental approach in infants/children/adolescents and Gross Motor Function Measure (GMFM)	MEDLINE and EMBASE between January 1996 and July 2007	conventional therapy was the focus; intensive (>3 times/week) vs. nonintensive rehabilitative treatment GMFM change score was higher for intensive treatment group compared with nonintensive treatment group effect of intensive treatment tended to be stronger for children who were 2 years old or younger GMFM change score did not differ for treatment that lasted less than 60 days
Hoare et al.[15]	2010	All RCTs comparing BoNT-A injection or BoNT-A injection plus occupational therapy in upper limbs with other treatments (includes no treatment or placebo). 10 trials met inclusion criteria.	Cochrane Library (Issue 3, 2008); MEDLINE (1966—2008 August Week 1); EMBASE (1980—2008 Week 28); CINAHL (1982—August Week 1 2008)	BoNT-A injections or BoNT-A and occupational therapy in the treatment of the upper limb in children with CP. Evidence supports use of BoNT-A as an adjunct to managing the upper limb in children with spastic CP. BoNT-A should not be used in isolation, but with other planned occupational therapy. Further research: Identify children most likely to respond to BoNT-A injections, monitor longitudinal outcomes, determine timing and effect of repeated injections, and most effective dosage, dilution and volume schedules.
Scianni et al.[16]	2009	Random allocation, concealed allocation, groups similar at baseline, participant blinding, therapist blinding, assessor blinding, < 15% dropouts, intention-to-treat analysis, between group difference reported, point estimate and variability reported	MEDLINE (1966—July 2008); CINAHL (1982—July 2008); EMBASE (1974—July 2008); PEDro (through July 2008)	Strengthening interventions that involved repetitive, strong, or effortful muscle contractions and progressed as ability changed, such as biofeedback, electrical stimulation, and progressive resistance exercise. In children and adolescents with CP who are walking, muscle strengthening is not effective in children and adolescents with CP Future research: investigating muscle strengthening at high intensities in children and adolescents with CP with lower levels of activity may be useful to guide clinical practice.

Table C-2. Meta-analyses—treatment of CP & other (continued)

Reference	Year	Inclusion/Exclusion Criteria	Search Dates	Summary of treatment or other
Sakzewki et al.[17]	2009	• Systematic reviews either with or without meta-analyses and randomized or quasi-randomized controlled trials • children aged 0 to 18 years with congenital hemiplegia with spasticity affecting upper limb function • interventions to improve upper limb function and participation were nonsurgical • Papers were excluded if trials were nonrandomized or had no control group, participants did not include a subset of children with hemiplegia, outcomes reported were impairment only, or studies not published in English.	MEDLINE (1950—July 2008); CINAHL (1982—July 2008); EMBASE (1998 —July 2008); AMED (1985—July 2008); PsycINFO (1967—July 2008); Web of Science (1945—July 2008)	• therapeutic management of upper-limb (UL) dysfunction in children with congenital hemiplegia • Interventions that address UL dysfunction in children with hemiplegia are varied—no one treatment seems to be superior. However, growing evidence that BoNT-A injections provide a supplementary benefit to a variety of upper limb training approaches. • Future research: Suitably powered RCTs using valid and reliable outcome measures necessary to determine efficacy of UL interventions. Investigation of minimum dosage of interventions for exact treatment required to optimize research.
Albavera-Hernandez et al.[18]	2009	• study of patients under 18 years of age • randomized clinical controlled trial epidemiological design • intramuscular injection with BoNT-A (Botox, Dysport and/or Xeomin) treatment of spasticity secondary to CP • administration of placebo and/or rehabilitation in comparison group to ensure better counterfactual design. • exclusion criteria: botulinum toxin type B excluded because of the more frequent autonomic adverse effects, despite the fact that its biological activity is less than BoNT-A.	MEDLINE (January 1990—February 2008)	• BoNT-A among children with spasticity secondary to CP • Occurrence of adverse events with BoNT-A is more frequent among children with CP than individuals with other conditions. • Severe adverse events potentially related with the use of BoNT-A, but data sparse and additional study require to clarify causal relation. BoNT-A has a good short-term safety profile, but further use should be strictly monitored using specific pharmaco-epidemiological surveillance systems.

Table C-2. Meta-analyses—treatment of CP & other (continued)

Reference	Year	Inclusion/Exclusion Criteria	Search Dates	Summary of treatment or other
Simpson et al.[19]	2008	No inclusion/exclusion criteria provided	MEDLINE and Current Contents (up to April 2007)	botulinum neurotoxin for the treatment of spasticity botulinum neurotoxin should be offered as a treatment option for the treatment of spasticity in adults and children future research: Studies should investigate factors that predict which patient subgroups have optimal response. further studies on injection methodology including use of EMG guidance, ultrasonography, and electrical stimulation to optimize treatment technique Research needed to determine optimal dose of BoNT-A for individual muscles and the choice of the number and location of injection sites. Studies also needed to assess the safety and efficacy of repeated and long-term injections of BoNT-A and to address the risk of development of secondary resistance to BoNT-A due to antibody formation.
Hoare et al.[26]	2007	All RCTs and controlled clinical trials (CCT) comparing constraint-induced movement therapy (CIMT), modified CIMT and Forced Use with traditional services (occupational therapy, physiotherapy, or no therapy).	Cochrane Library (Issue 3, 2006); MEDLINE (1966—2006 August Week 4); CINAHL (1982—2006 July Week 3); EMBASE (1980—August 2006); PsychInfo (1985—2006 August Week 4)	CIMT, modified CIMT, and Forced Use should be considered experimental in children with hemiplegic CP due to limited evidence. Future research: appropriately powered studies with uniform and objective outcome measures to allow pooling of data in future meta analyses; outcomes that measure usefulness of affected upper limb in bimanual tasks (ex. Assisting Hand Assessment) and individual goal setting (ex. Canadian Occupational Performance Measure and Goal Attainment Scaling); investigations to pursue longer-term outcomes and individual characteristics of children who experience positive CIMT outcomes.
Hoare et al.[53]	2007	All RCTs and CCTs comparing CIMT, modified CIMT, and Forced Use with traditional services such as occupational therapy, physiotherapy, or no treatment.	Cochrane Library (Issue 3, 2006); MEDLINE (1966—2006 August Week 4); CINAHL (1982—2006 July Week 3); EMBASE (1980—August 2006); PsychInfo (1985—2006 August Week 4)	Significant treatment effect found using modified CIMT in one trial. Positive trend favoring CIMT and Forced Use. Limited evidence, therefore use of CIMT, modified CIMT, and Forced Use should be considered experimental in children with hemiplegic CP.

Table C-2. Meta-analyses—treatment of CP & other (continued)

Reference	Year	Inclusion/Exclusion Criteria	Search Dates	Summary of treatment or other
Lannin et al.[20]	2006	Studies used focused on the effect of therapy on motor control, functional abilities, contracture, spasticity, and/or pain.	MEDLINE (1956—September 2003); CINAHL (1983—September 2003); EMBASE (1980—September 2003)	therapy for children with CP after BoNT-A injections Insufficient evidence to either support or refute use of therapy interventions after BoNT-A injections in children with CP. Future research: scarcity of evidence for use of therapy after BoNT-A injections in children with CP, further trials using appropriate methods are required before conclusions can be drawn about effectiveness of individual therapy interventions.
Cardoso et al.[21]	2006	Double-blind, placebo-controlled, randomized clinical trials evaluating the safety and efficacy of BoNT-A for treatment of equinus foot due to spasticity in CP (1980—2004) Children studied between ages 2—16	1980 (year botulinum toxin in humans approved by FDA)—2004	BoNT-A for treatment of spastic equinus foot in CP Treatment of patients with spastic equinus foot in CP with BoNT-A resulted in statistically significant gait improvement with minor side effects. Studies in this meta-analysis demonstrated major outcomes through medical evaluation and video gait analyses (both had many aspects of subjectivity). Some authors have also argued about the associated improvement in function or quality of life in these patients after BoNT-A. Final outcome is posture/gait improvement, but formal evidence is still lacking in order to establish the real benefit of physical and occupational therapy in the rehabilitation of equinus foot patients.
Harris & Roxborough[22]	2005	Only physical therapy interventions included (adaptive seating devices, ankle foot orthoses, neurodevelopmental treatment (NDT)).	1990—2004	Physical therapy in enhancing postural control in children with CP Future research: Additional studies with stronger designs needed to establish that postural control interventions for children with CP are effective.

Table C-2. Meta-analyses—treatment of CP & other (continued)

Reference	Year	Inclusion/Exclusion Criteria	Search Dates	Summary of treatment or other
Siebes et al.[23]	2002	only original articles published in English, German, Spanish, or French in a (Social) Science Citation Index, S(S)CI, journal participants were groups of children at risk for or diagnosed with CP and who were aged from 0-18 years at the start of the program only studies that used currently accepted clinically based traditional therapeutic motor intervention methods or a combination of these methods and other forms of therapy were included adjuncts to physical therapy, such as botulinum injection therapy, intrathecal baclofen, and orthopedic devices, were excluded articles on oral motor control, surgical interventions, pharmacotherapeutical interventions, dental care, nutrition, acupuncture, psychotherapy, and hyperbaric oxygen therapy were excluded long-term follow-up studies were only included if the program characteristics of the original study were described in sufficient detail	Jan 1990-Apr 2001	• therapeutic motor intervention programmes for children with or at risk for CP • among the 49 studies in the review, NDT, conductive education, electrical stimulation, strength training, biofeedback, hippotherapy, and saddle riding were most frequently evaluated • only 4 studies included more than 50 patients children with quadriplegia were the predominant participants, followed by children with hemiplegia and diplegia • most therapies were center-based and carried out by a physical therapist on a one-one basis (parent involvement mentioned in 20 studies) ranging from once/week to daily, from one session to more than 2 years, from 5 minutes to a full school day • of the 49 studies, 20 used control or contrast groups, 15 used random assignment • methodology and quality of studies improved over time, however, due to a lack of positive findings, these developments did not lead to a substantial improvement in the scientific foundation of the interventions under study • majority of studies in review were short-term, so future research should focus on long-term effects mainly • little research to assess or evaluate the efficacy of therapeutic motor intervention programs for children with CP

Table C-2. Meta-analyses—treatment of CP & other (continued)

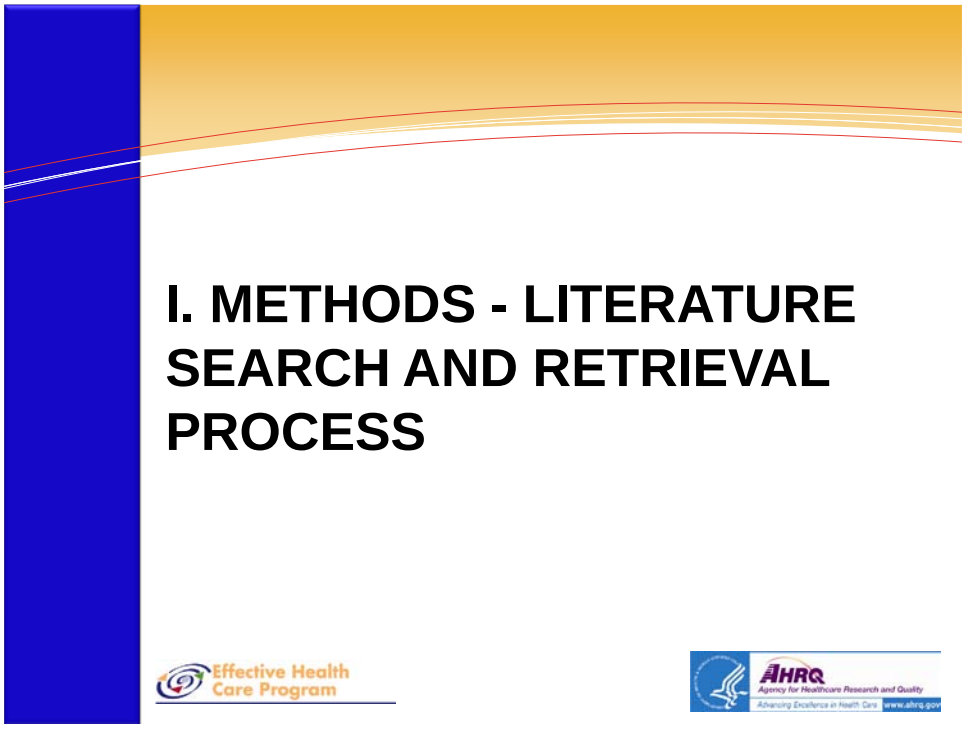
Reference	Year	Inclusion/Exclusion Criteria	Search Dates	Summary of treatment or other
Morris[24]	2002	studies were included if they involved any clearly described scientific methodology that compared a lower limb orthosis with a control group or no orthoses for children with CP abstracts were included because few studies had been published as journal articles studies were excluded if they examined heterogeneous diagnoses such as adults, or children with head injuries interventions such as temporary applications of casts were also excluded	1994-2000	• lower-limb orthoses used for CP • one prospective RCT, otherwise uniformly within-participant comparisons (5 prospective, 17 cross-sectional, and 4 retrospective) • children most commonly spastic type CP • descriptions of types of orthoses were inconsistent which made it difficult to know what movements were being permitted or restricted • effect of footwear on performing activities with or without orthosis and sensitivity and accuracy of measurement technique may have distorted some of the findings • GMFM used the heterogeneous research designs and different types of orthoses used preclude any kind of statistical aggregation of the outcomes that may otherwise help when only small numbers have been included • improvement commonly reported using any orthoses compared with the barefoot condition
McLaughlin et al.[25]	2002	RCTs with children with spastic diplegia receiving SDR plus physiotherapy or physiotherapy without SDR	1997-1998	• SDR for the treatment of CP • SDR consistently reduces or eliminates spasticity • difference in functional outcome with 2 studies showing a statistically significant advantage for SDR and the 3rd showing no advantage • small but statistically significant advantage to SDR plus physical therapy compared with physical therapy-only that is independent of any site-specific diff among the studies • a sizable well-studied cohort of individuals with spastic diplegia should be followed to adulthood
Kunz et al.[27]	2006	• children younger than 20 years of age • disease defined by pediatric professionals • NDT programs, physical activity, strength training, conductive education, functional or sensory integration therapy • systematic reviews, health technology assessment reports, or guidelines. 15 RCTs finally included in the methodology project.	MEDLINE (1966—June 2003); Cochrane Library (until February 2003); ACP Journal Club (1991—January 2003); CINAHL (1982—June 2003)	• methodological quality in physiotherapy trials in childhood CP • This review indicates that good quality RCTs on the effectiveness of complex interventions are feasible. Clinical heterogeneity of CP a major challenge in performance and interpretation of clinical trials. • Future research: Possible need for a broader understanding of "standardization," since not all studies provide informative baseline characteristics. More work is needed to tackle methodological weaknesses, such as ensuring adequate reporting to facilitate transfer of findings into routine care.

Appendix D. Slide Presentation from In-Person Forum

Slide 1

Methods—Literature Search and Retrieval Process

All slides have the logo of the Effective Health Care Program, AHRQ. Agency for Healthcare Research and Quality, and the Department of Health and Human Services.



All slides have the logo of the Effective Health Care Program, AHRQ. Agency for Healthcare Research and Quality, and the Department of Health and Human Services.

Slide 2

Literature Search

- We identified existing systematic reviews, guidelines, and meta-analyses.
- Research foci and outcomes not found in our search, but considered important by stakeholders, may be priorities for future systematic reviews.

Slide 3

Search Terms

Our initial search included:

1. Spastic diplegia, quadriplegia, and hemiplegia
2. Congenital diplegia, quadriplegia, and hemiplegia
3. Static encephalopathy
4. Choreoathetosis

Slide 4

Search Terms

A second search added content identified in the stakeholder calls

1. Psychotherapy
2. Physical fitness
3. Quality of life, Transitions
4. Pain, Comorbidities
5. Cultural diversity
6. Follow-up studies
7. Technologies

Slide 5

Article Selection

- 104* guidelines, consensus statements, meta-analyses, and systematic reviews
  - 76 systematic reviews
  - 14 guidelines and consensus statements
  - 14 meta-analyses pertaining to treatment

* Total number of papers depicted in graphs that follow is greater than number stated here because most papers are relevant to multiple treatment target areas

- Reviewing the literature revealed a number of treatment targets by which we organized the references

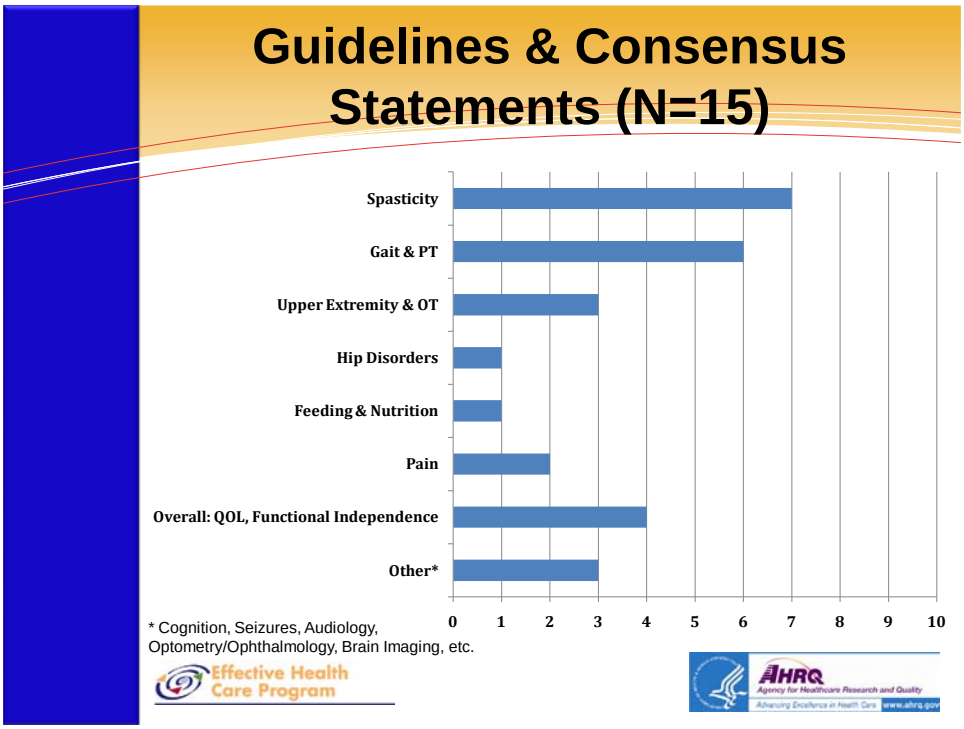
Slide 6

Article Selection (cont.)

- 2,602 publications of primary research
  - Approximately 500 added from our second search that included new key terms
  - Despite the absence of reviews in areas recommended by stakeholders, primary literature does exist and warrants exploration for systematic review topics.

Slide 7

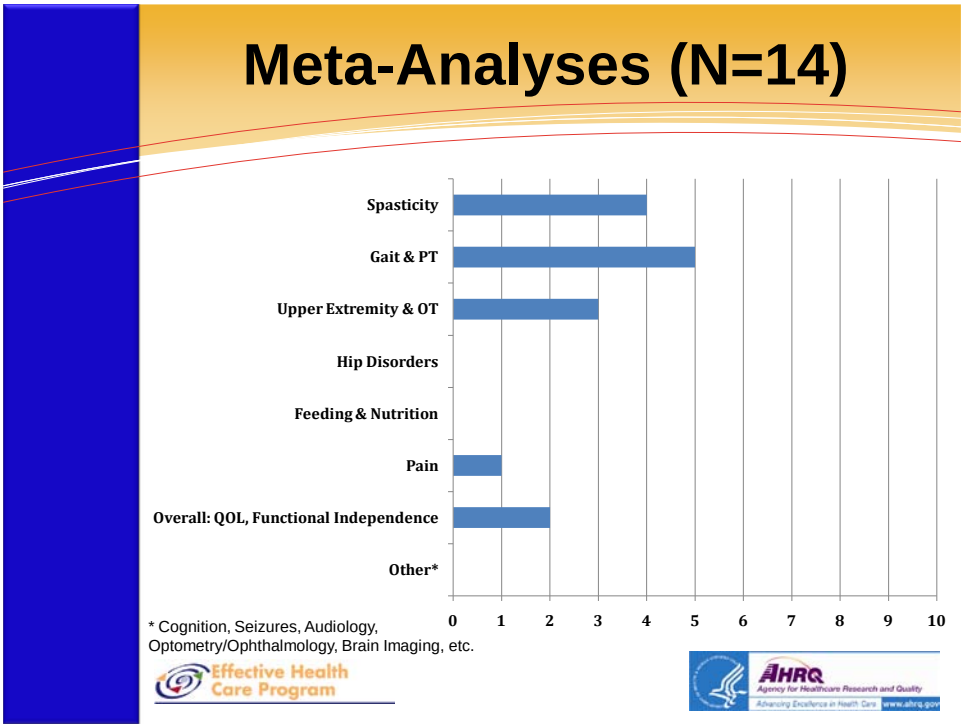
Guidelines & Consensus Statements (N=14)



- Spasticity: 7
- Gait & PT: 6
- Upper Extremity & OT: 3
- Hip Disorders: 1
- Feeding & Nutrition: 1
- Pain: 2
- Overall: QOL, Functional Independence: 4
- Other (Cognition, Seizures, Audiology, Optometry/Ophthalmology, Brain Imaging, etc.): 3

Slide 8

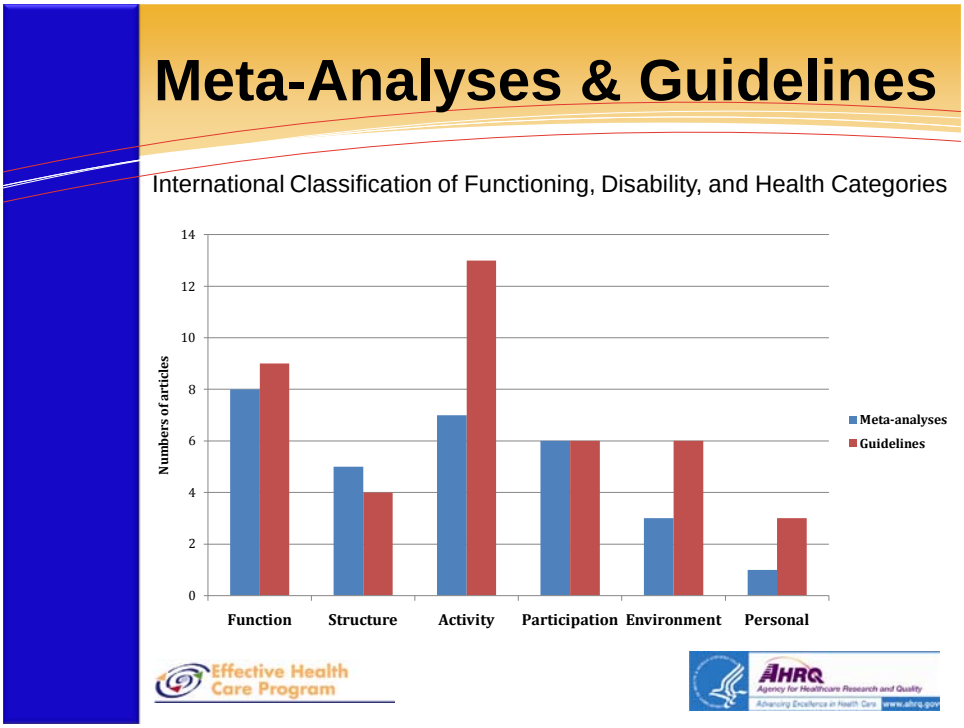
Meta-Analyses (N=14)



- Spasticity: 4
- Gait & PT: 5
- Upper Extremity & OT: 3
- Hip Disorders: —
- Feeding & Nutrition: —
- Pain: 1
- Overall: QOL, Functional Independence: 2
- Other (Cognition, Seizures, Audiology, Optometry/Ophthalmology, Brain Imaging, etc.): —

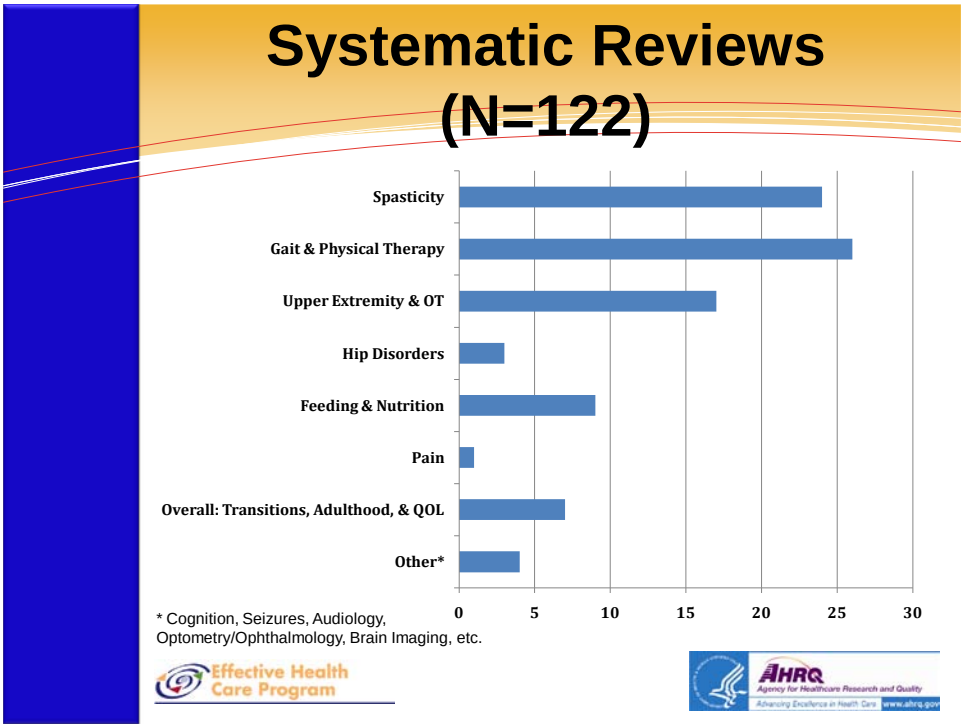
Slide 9

Meta-Analyses and Guidelines



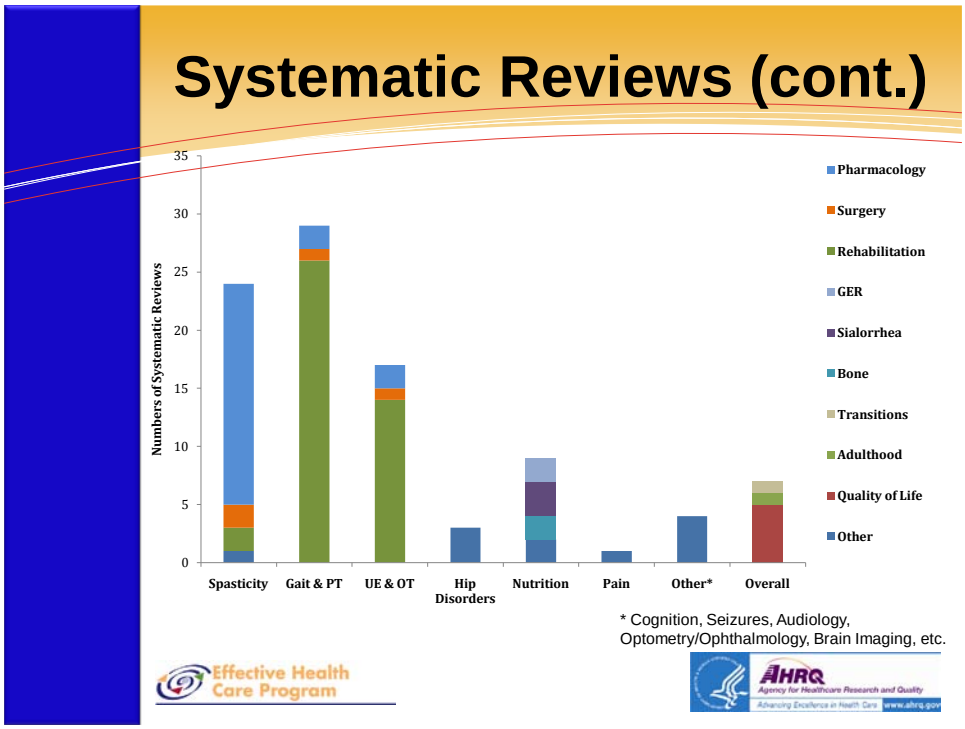
Slide 10

Systematic Reviews (N=122)



Slide 11

Systematic Reviews (cont.)



	Spasticity	Gait & PT	Upper Extremity & OT	Hip Disorders	Nutrition	Pain	Other*	Overall
Pharmacology								
Surgery		1	1					
Rehabilitation								
GER					2			
Sialorrhea					3			
Bone	19	2	2		2			
Transitions								1
Adulthood	2	27	14					1
Quality of Life	2							5
Other	1			4	2	1	4	

* Cognition, Seizures, Audiology, Optometry/Ophthalmology, Brain Imaging, etc.

Slide 12

Systematic Reviews (cont.)

International Classification of Functioning, Disability, and Health Categories

Categories	Numbers of systematic reviews
Function	48
Structure	19
Activity	52
Participation	24
Environment	15
Personal	9

Slide 13

- PICOTS

Slide 14

PICOTS

- A tool to help us characterize the research areas and questions that you identify and prioritize
- Additional information to guide our research, both systematic reviews and primary research

Slide 15

PICOTS

P: Populations
I: Interventions
C: Comparators
O: Outcomes
T: Timing
S: Setting

Slide 16

Definitions

- Population —condition, disease severity and stage, comorbidities, patient demographics
- Intervention—dosage, frequency, and method of administration
- Comparator—placebo, usual care, or active control
- Outcome—health outcomes, morbidity, mortality, QoL
- Timing–duration of follow-up
- Setting—primary, specialty, in-patient, co-interventions

Slide 17

Example Questions to Think About

- Is there epidemiologic or etiologic information needed before interventions can be assessed?
- What is the intervention of interest?
- What is the relevant population?
- What is the ideal comparison?
- What outcomes are relevant?
- Where does the intervention take place?
- Are there methodologic challenges to understanding the clinical question at hand?

Appendix E. Description of the Treatment Targets and the Organizing Framework

A simplified conceptual framework can be very helpful for organizing the large body of knowledge that has been reported about cerebral palsy. For the purposes of this project, the International Classification of Functioning, Disability and Health (ICF) will be used to illustrate the breadth and depth of this topic.[54] The purpose of this classification system is to take a biologic, personal, and social perspective on the state of an individual's health and disability. An individual's function, disability and health can only be described by taking a cross-section that includes body structure, body function, activity, and personal environment.

Because of the current structure of available scientific research and for the sake of practicality we will focus on each treatment target separately. The following treatment targets represent a cross-section of the functionalities that would directly affect the health and disability of a patient with CP:

A. Spasticity
B. Gait and Physical Therapy
C. Upper Extremity and Occupational Therapy
D. Hip Disorders
E. Feeding and Nutrition Problems
F. Pain
G. Other: Cognition, Seizures, Audiology, Optometry/Ophthalmology, Brain Imaging, etc.
H. Overall: Quality of Life, Functional Independence, Transitions, etc.

Here we present a survey of the evidence (i.e. meta-analyses, systematic reviews, and practice guidelines) for each treatment target. Furthermore, we fit the information for each treatment target into the following organizing framework:

1. the availability of strategies to reduce burden (treatments and prevention);
2. variations in prevalence, diagnosis, age distribution, sociodemographic measures, interventions, outcomes, service delivery, management strategies, clinical practice, provisions of services, and the availability of care;
3. uncertainties regarding outcomes, methodology, diagnosis, treatment, and payor issues;
4. emerging interventions and approaches to management; and
5. paradigm shifts.

The focus on treatment targets does not preclude the future analysis of a framework category going across multiple treatment targets. For example, do variations in the diagnostic criteria for spasticity cause delays in seeking rehabilitative therapies and negatively affect functional independence? The fruitful discussion of stakeholders within the Issues Exploration Forum will identify practical questions like this that could warrant systematic review or further investigations.

The significance of each treatment topic will be discussed at the beginning of each treatment target's framework. Systematic reviews for each treatment target for CP are listed in Table E-1.

Table E-1. Existing systematic reviews by treatment target

Treatment Target	Systematic Reviews
Spasticity	Ade-Hall RA and Moore AP. Botulinum toxin type A in the treatment of lower limb spasticity in cerebral palsy. Boyd RN and Hays RM. Current evidence for the use of botulinum toxin type A in the management of children with cerebral palsy: a systematic review. Eur J Neurol. 2001 Nov;8 Suppl 5:1-20. Butler C and Campbell S. Evidence of the effects of intrathecal baclofen for spastic and dystonic cerebral palsy. AACPDM Treatment Outcomes Committee Review Panel. Dev Med Child Neurol. 2000 Sep;42(9):634-45. Cardoso ES, Rodrigues BM, Barroso M, et al. Botulinum toxin type A for the treatment of the spastic equinus foot in cerebral palsy. Pediatr Neurol. 2006 Feb;34(2):106-9. Dodd KJ, Taylor NF and Damiano DL. A systematic review of the effectiveness of strength-training programs for people with cerebral palsy. Arch Phys Med Rehabil. 2002 Aug;83(8):1157-64. Edgar TS. Clinical utility of botulinum toxin in the treatment of cerebral palsy: comprehensive review. J Child Neurol. 2001 Jan:16(1): 37-46. Gordon MF and Barron R. Effectiveness of repeated treatment with botulinum toxin type A across different conditions. South Med J. 2006 Aug;99(8):853-61. Heinen F, Deslovere K, Schroeder AS, et al. The updated European Consensus 2009 on the use of Botulinum toxin for children with cerebral palsy. Eur J Paediatr Neurol. 2010 Jan;14(1):45-66. Heinen F, Molenaers G, Fairhurst C, et al. European consensus table 2006 on botulinum toxin for children with cerebral palsy. Eur J Paediatr Neurol. 2006 Sep-Nov;10(5-6):215-25. Hoare BJ and Imms C. Upper-limb injections of botulinum toxin-A in children with cerebral palsy: a critical review of the literature and clinical implications for occupational therapists. Am J Occup Ther. 2004 Jul-Aug;58(4):389-97. Hoare BJ and Imms C, et al. Constraint-induced movement therapy in the treatment of the upper limb in children with hemiplegic cerebral palsy: a Cochrane systematic review. Clin Rehabil. 2007 Aug:21(8): 675-85. Hoare BJ, Wallen MA, Imms C, et al. Botulinum toxin A as an adjunct to treatment in the management of the upper limb in children with spastic cerebral palsy (UPDATE). Cochrane Database Syst Rev. 2010(1):CD003469. Lannin N, Scheinberg A and Clark K. AACPDM systematic review of the effectiveness of therapy for children with cerebral palsy after botulinum toxin A injections. Dev Med Child Neurol. 2006 Jun;48(6):533-9. Lukban MB, Rosales RL and Dressler D. Effectiveness of botulinum toxin A for upper and lower limb spasticity in children with cerebral palsy: a summary of evidence. J Neural Transm. 2009 Mar;116(3):319-31. Montane E, Vallano A and Laporte JR. Oral antispastic drugs in nonprogressive neurologic diseases: a systematic review. Neurology. 2004 Oct 26;63(8):1357-63. Park ES and Rha DW. Botulinum toxin type A injection for management of upper limb spasticity in children with cerebral palsy: a literature review. Yonsei Med J. 2006 Oct 31;47(5):589-603. Pin T, Dyke P and Chan M. The effectiveness of passive stretching in children with cerebral palsy. Dev Med Child Neurol. 2006 Oct;48(10):855-62. Reeuwijk A, van Schie PE, Becher JG, et al. Effects of botulinum toxin type A on upper limb function in children with cerebral palsy: a systematic review. Clin Rehabil. 2006 May;20(5):375-87. Sakzewski L, Ziviani J and Boyd R. Systematic review and meta-analysis of therapeutic management of upper-limb dysfunction in children with congenital hemiplegia. Pediatrics. 2009 Jun;123(6):e1111-22.

Table E-1. Existing systematic reviews by treatment target (continued)

Treatment Target	Systematic Reviews
Spasticity (continued)	Simpson DM, Gracies JM, Graham HK, et al. Assessment: Botulinum neurotoxin for the treatment of spasticity (an evidence-based review): report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Neurology. 2008 May 6;70(19):1691-8. Smeulders M, Coester A and Kreulen M. Surgical treatment for the thumb-in-palm deformity in patients with cerebral palsy. Cochrane Database Syst Rev. 2005(4):CD004093. Wasiak J, Hoare B and Wallen M. Botulinum toxin A as an adjunct to treatment in the management of the upper limb in children with spastic cerebral palsy. Cochrane Database Syst Rev. 2004(4):CD00346
Gait & Physical Therapy	Anttila H, Autti-Ramo I, Suoranta J, et al. Effectiveness of physical therapy interventions for children with cerebral palsy: a systematic review. BMC Pediatr. 2008;8:14. Blackmore AM, Boettcher-Hunt E, Jordan M, et al. A systematic review of the effects of casting on equinus in children with cerebral palsy: an evidence report of the AACPDM. Dev Med Child Neurol. 2007 Oct;49(10):781-90. Butler C and Darrah J. Effects of neurodevelopmental treatment (NDT) for cerebral palsy: an AACPDM evidence report. Dev Med Child Neurol. 2001 Nov;43(11):778-90. Butler JM, Scianni A and Ada L. Effect of cardiorespiratory training on aerobic fitness and carryover to activity in children with cerebral palsy: a systematic review. Int J Rehabil Res. 2010 Jun;33(2):97-103. Damiano DL and DeJong SL. A systematic review of the effectiveness of treadmill training and body weight support in pediatric rehabilitation. J Neurol Phys Ther. 2009 Mar;33(1):27-44. Figueiredo EM, Ferreira GB, Maia Moreira RC, et al. Efficacy of ankle-foot orthoses on gait of children with cerebral palsy: systematic review of literature. Pediatr Phys Ther. 2008 Fall;20(3):207-23. Glinsky J, Harvey L and Van Es P. Efficacy of electrical stimulation to increase muscle strength in people with neurological conditions: a systematic review. Physiother Res Int. 2007 Sep;12(3):175-94. Hailey D and Tomie J. An assessment of gait analysis in the rehabilitation of children with walking difficulties. Disabil Rehabil. 2000 Apr 15;22(6):275-80. Houltram J, Noble I, Boyd RN, et al. Botulinum toxin type A in the management of equinus in children with cerebral palsy: an evidence-based economic evaluation. Eur J Neurol. 2001 Nov;8 Suppl 5:194-202. Kerr C, McDowell B and McDonough S. Electrical stimulation in cerebral palsy: a review of effects on strength and motor function. Dev Med Child Neurol. 2004 Mar;46(3):205-13. Lannin N, Scheinberg A and Clark K. AACPDM systematic review of the effectiveness of therapy for children with cerebral palsy after botulinum toxin A injections. Dev Med Child Neurol. 2006 Jun;48(6):533-9. Mockford M and Caulton JM. Systematic review of progressive strength training in children and adolescents with cerebral palsy who are ambulatory. Pediatr Phys Ther. 2008 Winter;20(4):318-33. Mattern-Baxter K. Effects of partial body weight supported treadmill training on children with cerebral palsy. Pediatr Phys Ther. 2009 Spring;21(1):12-22. Morris C. A review of the efficacy of lower-limb orthoses used for cerebral palsy. Dev Med Child Neurol. 2002 Mar;44(3):205-11. Mutlu A, Krosschell K and Spira DG. Treadmill training with partial body-weight support in children with cerebral palsy: a systematic review. Dev Med Child Neurol. 2009 Apr;51(4):268-75. Paul SM, Siegel KL, et al. Evaluating interventions to improve gait in cerebral palsy: a meta-analysis of spatiotemporal measures. Dev Med Child Neurol. 2007 Jul;49(7):542-549. Pin TW. Effectiveness of static weight-bearing exercises in children with cerebral palsy. Pediatr Phys Ther. 2007 Spring;19(1):62-73.

Table E-1. Existing systematic reviews by treatment target (continued)

Treatment Target	Systematic Reviews
Gait & Physical Therapy (continued)	Rogers A, Furler BL, Brinks S, et al. A systematic review of the effectiveness of aerobic exercise interventions for children with cerebral palsy: an AACPDM evidence report. Dev Med Child Neurol. 2008 Nov;50(11):808-14. Seifart A, Unger M and Burger M. The effect of lower limb functional electrical stimulation on gait of children with cerebral palsy. Pediatr Phys Ther. 2009 Spring;21(1):23-30. Simpson DM, Gracies JM, Graham HK, et al. Assessment: Botulinum neurotoxin for the treatment of spasticity (an evidence-based review): report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Neurology. 2008 May 6;70(19):1691-8. Steinbok P. Outcomes after selective dorsal rhizotomy for spastic cerebral palsy. Childs Nerv Syst. 2001 Jan;17(1-2):1-18. Steultjens EM, Dekker J, Bouter LM, et al. Occupational therapy for children with cerebral palsy: a systematic review. Clin Rehabil. 2004 Feb;18(1):1-14. Taylor NF, Dodd, KJ, et al. Progressive resistance exercise in physical therapy: a summary of systematic reviews. Phys Ther. 2005 Nov;85(11):1208-23. Verschuren O, Ketelaar M, Takken T, et al. Exercise programs for children with cerebral palsy: a systematic review of the literature. Am J Phys Med Rehabil. 2008 May;87(5):404-17. Willoughby KL, Dodd KJ and Shields N. A systematic review of the effectiveness of treadmill training for children with cerebral palsy. Disabil Rehabil. 2009;31(24):1971-9.

Table E-1. Existing systematic reviews by treatment target (continued)

Treatment Target	Systematic Reviews
Upper Extremity & Occupational Therapy	Anttila H, Malmivaara A, Kunz R, et al. Quality of reporting of randomized, controlled trials in cerebral palsy. Pediatrics. 2006 Jun;117(6):2222-30. Anttila H, Suoranta J, Malmivaara A, et al. Effectiveness of physiotherapy and conductive education interventions in children with cerebral palsy: a focused review. Am J Phys Med Rehabil. 2008 Jun;87(6):478-501. Boyd RN, Morris ME and Graham HK. Management of upper limb dysfunction in children with cerebral palsy: a systematic review. Eur J Neurol. 2001 Nov;8 Suppl 5:150-66. Chung J, Evans J, Lee C, et al. Effectiveness of adaptive seating on sitting posture and postural control in children with cerebral palsy. Pediatr Phys Ther. 2008 Winter;20(4):303-17. Hoare B, Imms C, Carey L, et al. Constraint-induced movement therapy in the treatment of the upper limb in children with hemiplegic cerebral palsy: a Cochrane systematic review. Clin Rehabil. 2007 Aug;21(8):675-85. Hoare BJ, Wasiak J, Imms C, et al. Constraint-induced movement therapy in the treatment of the upper limb in children with hemiplegic cerebral palsy. Cochrane Database Syst Rev. 2007(2):CD004149. Huang HH, Fetters L, Hale J, et al. Bound for success: a systematic review of constraint-induced movement therapy in children with cerebral palsy supports improved arm and hand use. Phys Ther. 2009 Nov;89(11):1126-41. Lannin NA, Novak I and Cusick A. A systematic review of upper extremity casting for children and adults with central nervous system motor disorders. Clin Rehabil. 2007 Nov;21(11):963-76. McDonagh MS, Morgan D, Carson S, et al. Systematic review of hyperbaric oxygen therapy for cerebral palsy: the state of the evidence. Dev Med Child Neurol. 2007 Dec;49(12):942-7 Michael SM, Porter D and Pountney TE. Tilted seat position for non-ambulant individuals with neurological and neuromuscular impairment: a systematic review. Clin Rehabil. 2007 Dec;21(12):1063-74. Sakzewski L, Ziviani J and Boyd R. Systematic review and meta-analysis of therapeutic management of upper-limb dysfunction in children with congenital hemiplegia. Pediatrics. 2009 Jun;123(6):e1111-22 Sterba JA. Does horseback riding therapy or therapist-directed hippotherapy rehabilitate children with cerebral palsy? Dev Med Child Neurol. 2007 Jan;49(1):68-73. Steultjens EM, Dekker J, Bouter LM, et al. Evidence of the efficacy of occupational therapy in different conditions: an overview of systematic reviews. Clin Rehabil. 2005 May;19(3):247-54. van Munster JC, Maathuis KG, Haga N, et al. Does surgical management of the hand in children with spastic unilateral cerebral palsy affect functional outcome? Dev Med Child Neurol. 2007 May;49(5):385-9.
Hip Disorders	Gordon GS and Simkiss DE. A systematic review of the evidence for hip surveillance in children with cerebral palsy. J Bone Joint Surg Br. 2006 Nov;88(11):1492-6. Pountney T and Green EM. Hip dislocation in cerebral palsy. BMJ. 2006 Apr 1;332(7544):772-5 Stott NS and Piedrahita L. Effects of surgical adductor releases for hip subluxation in cerebral palsy: an AACPDM evidence report. Dev Med Child Neurol. 2004 Sep;46(9):628-45.

Table E-1. Existing systematic reviews by treatment target (continued)

Treatment Target	Systematic Reviews
Feeding & Nutrition Problems	Cohen M, Lahat E, Bistritzer T, et al. Evidence-based review of bone strength in children and youth with cerebral palsy. J Child Neurol. 2009 Aug;24(8):959-67. Fuster Torres MA, Berini Aytes L and Gay Escoda C. Salivary gland application of botulinum toxin for the treatment of sialorrhea. Med Oral Patol Oral Cir Bucal. 2007 Dec;12(7):E511-7 Hough JP, Boyd RN and Keating JL. Systematic review of interventions for low bone mineral density in children with cerebral palsy. Pediatrics. 2010 Mar;125(3):e670-8. Samson-Fang L, Butler C and O'Donnell M. Effects of gastrostomy feeding in children with cerebral palsy: an AACPDM evidence report. Dev Med Child Neurol. 2003 Jun;45(6):415-26. Sleigh G and Brocklehurst P. Gastrostomy feeding in cerebral palsy: a systematic review. Arch Dis Child. 2004 Jun;89(6):534-9. Tscheng DZ. Sialorrhea—therapeutic drug options. Ann Pharmacother. 2002 Nov;36(11):1785-90. Vaile L and Finlay F. Is injection of botulinum toxin type A effective in the treatment of drooling in children with cerebral palsy? Arch Dis Child. 2006 Oct;91(10):862-3. Vernon-Roberts A and Sullivan PB. Fundoplication versus post-operative medication for gastro-oesophageal reflux in children with neurological impairment undergoing gastrostomy. Cochrane Database Syst Rev. 2007(1):CD006151.
Pain	Swiggum M, Hamilton ML, Gleeson P, et al. Pain in children with cerebral palsy: implications for pediatric physical therapy. Pediatr Phys Ther. 2010 Spring;22(1):86-92.
Other—Cognition, Seizures, Audiology, Optometry/ Ophthalmology, Brain Imaging, etc.	Darrah J, Watkins B, Chen L, et al. Conductive education intervention for children with cerebral palsy: an AACPDM evidence report. Dev Med Child Neurol. 2004 Mar;46(3):187-203. Korzeniewski SJ, Birbeck G, et al. A systematic review of neuroimaging for cerebral palsy. J Child Neurol. 2008 Feb; 23(2): 216-227. Krach LE. Pharmacotherapy of spasticity: oral medications and intrathecal baclofen. J Child Neurol. 2001 Jan;16(1):31-6. Pennington L, Goldbart J and Marshall J. Interaction training for conversational partners of children with cerebral palsy: a systematic review. Int J Lang Commun Disord. 2004 Apr-Jun;39(2):151-70. Pennington L, Goldbart J and Marshall J. Speech and language therapy to improve the communication skills of children with cerebral palsy. Cochrane Database Syst Rev. 2004(2):CD003466.
Overall-Quality of Life, Functional Independence, Transitions, etc.	Albavera-Hernandez C, Rodriguez JM and Idrovo AJ. Safety of botulinum toxin type A among children with spasticity secondary to cerebral palsy: a systematic review of randomized clinical trials. Clin Rehabil. 2009 May;23(5):394-407. Binks JA, Barden WS, Burke TA, et al. What do we really know about the transition to adult-centered health care? A focus on cerebral palsy and spina bifida. Arch Phys Med Rehabil. 2007 Aug;88(8):1064-73. Heinen F, Desloovere K, Schroeder AS, et al. The updated European Consensus 2009 on the use of Botulinum toxin for children with cerebral palsy. Eur J Paediatr Neurol. 2010 Jan;14(1):45-66. Hoare BJ, Wallen MA, Imms C, et al. Botulinum toxin A as an adjunct to treatment in the management of the upper limb in children with spastic cerebral palsy (UPDATE). Cochrane Database Syst Rev. 2010(1):CD003469. Rapp CE, Jr. and Torres MM. The adult with cerebral palsy. Arch Fam Med. 2000 May;9(5):466-72.

Framework A: Spasticity

Spasticity is characterized by hyperreflexia and resistance to muscle lengthening (Table E-2).[10]Much of the morbidity associated with CP is directly or indirectly associated with spasticity. Spasticity results in decreased function, pain, deformity, and difficulty with caregiving.[6] While the clinical descriptions of CP emphasize the most prominent motor manifestation (i.e. spastic, dyskinetic, and ataxic), most CP patients have a mixture of these manifestations.[8] Subsequently, spasticity has been reported to affect up to 90 percent of patients with CP.[55] Potential morbidities associated with spasticity include contractures, decubitous ulcers, scoliosis, gait problems, nutrition problems, pain, fractures, and functional impairments. Reasons to treat spasticity include reducing pain and muscle spasms, facilitating brace use, improving posture, minimizing contractures and deformity, facilitating mobility and dexterity, and improving patient ease of care or self-care and hygiene.[7]

Although spasticity is a major focus in clinical practice there are a limited number of clinical trials to support current practices. The burden associated with CP can be addressed clinically by various treatment strategies and prevention strategies. The treatment strategies include stretching, daily range-of-motion exercises, weight bearing (standing), serial casting, bracing and orthotic devices, oral medications, intrathecal medication, specific nerve or motor blocks, dorsal rhizotomy, and orthopedic surgeries.[6,8] The goal of these interventions is to increase function, decrease disability, and facilitate mobility.[10] These treatment strategies can generally be divided into pharmacologic, surgical, and rehabilitative strategies. The typical approach is to combine multiple treatment strategies, for example, ankle-foot orthoses (AFO) and weekly physical therapy for a patient on oral baclofen. Evidence for the efficacy of many of these treatment strategies is mixed. Additionally, many of the most clinically important treatment strategies have little available evidence.

Pharmacologic Treatment Strategies

Reviews of the current evidence for pharmacologic treatment strategies are available from the American Academy of Neurology (AAN).[7,19]

Intramuscular botulinum toxin. Botulinum neurotoxin (BoNT) is considered as a therapy for localized or segmental spasticity (ex. calf spasticity, thigh adductor spasticity, and upper extremity spasticity). This localized approach is in contrast to the role of other pharmacologic therapies for generalized spasticity (e.g.,. oral baclofen or intrathecal baclofen). The level of evidence for BoNT differs with the anatomical location of therapy and several other variables. There is also variation in the dosing and dose equivalencies.

Oral anti-spasticity medications. Anti-spastic or spasmolytic agents, include medications that act on the central nervous system on synaptic neurotransmission or receptors like benzodiazepines (e.g., diazepam), oral baclofen, tizanidine, and gabapentin. Other medications like dantrolene directly affect muscle contractility.[12] There is insufficient evidence to support the efficacy of most of the oral anti-spasticity medications.

Intrathecal baclofen therapy. Compared to oral administration, intrathecal baclofen can provide a lower incidence of cerebral side effects and a greater reduction in tone.[12]The initial

implantation of the pump device and catheters requires a surgical procedure. The device and components require refilling and monitoring.

Surgical Treatment Strategies

Orthopedic surgeries. These surgeries include tendon lengthening, tendon transfer, bony osteotomy, and joint fusion.[10] There is variability in the ages recommended for surgeries.

Neurosurgical interventions. These surgeries include selective dorsal rhizotomy (SDR) and implantation of intrathecal baclofen pumps. There is variability in the indications and combinations of therapies recommended.

Rehabilitative Treatment Strategies

Rehabilitative treatment strategies include occupational therapy and physical therapy. More specific treatments include splinting, casting, strength training, constraint induced movement therapy (CIMT), neuromuscular electrical stimulation.[17] There are variations in the outcomes measured in this area: structure versus function versus activity limitation.

Prevention and Surveillance

Close surveillance for deformity to soft tissue or bony structures is recommended for patients with spasticity. This includes regular follow-up for physical exams and radiographs for specific groups of children with CP.[4]

Table E-2. Framework A: Spasticity

Issue	Examples
Availability of a strategy to reduce burden-Treatment	Treatment strategies include stretching, daily range-of-motion (ROM) exercises, weight bearing (standing), serial casting, bracing and orthotic devices, oral medications, intrathecal medication, specific nerve or motor blocks, SDR, and orthopedic surgeries.[6,8,10]
Availability of a strategy to reduce burden-Prevention	Prevention and surveillance strategies includes regular follow-up for physical exams and radiographs for specific groups of children with CP.[4]
Variations in prevalence among individuals with CP	There are variations in the estimations of prevalence of spasticity in individuals with CP but it is clearly a majority. Spasticity affects 75% of children with CP.[6] Spasticity affects 80-90% of individuals with CP.[55] Although the majority of patients with CP (at least 85%) are classified as having the "spastic" variety, there are very few patients with "pure" spasticity.[8] Between 66-82% of CP is the spastic type.[56] 93% of children with CP would develop dynamic or fixed deformity of foot or ankle according to study of 200 children with CP.[10]
Variations in issues of diagnosis	Two major issues in the diagnosis of CP are the variable expression of symptoms with patient age and the reliance on clinical description to classify the type of CP. *Patient age.* Variable expression of spasticity as patients age results in variations in the diagnosis of CP with age.[6] European Consensus of 2009 recommends re-classification of a child during every appointment, especially if the child is under 4 years old.[57] The pattern of distribution of spasticity may not stabilize until after 2 years old.[6] *Clinical Description*. Reliance on clinical classification by describing the anatomical distribution of spasticity results in some variation in diagnosis. Diagnosis of CP is a clinical determination based on history and physical exam and there is not a strict set of criteria or diagnostics. Signs of spasticity emerge in a variable manner and may even begin as hypotonia.[6]
Variations in age distributions	Variations in age distribution affect the estimates of prevalence, the expression of symptoms, and recommended treatments for spastic CP.[57] Instead of basing surgical interventions on age, they should be based on severity of spasticity, effect of spasticity, and patient size.[1] Questions remain about what ages are most optimal candidates for BoNT-A injections in the upper limb.[58]

Table E-2. Framework A: Spasticity (continued)

Issue	Examples
Variations in sociodemographic measures	None
Variations in interventions	There are variations in the intervention approaches to CP, with pharmacologic, surgical, and rehabilitation treatment strategies from which to choose. There is major variation in the selection of each therapy and in the appropriate combination of therapies. **Pharmacologic Treatment Strategies**: ***Intramuscular Botulinum Toxin***. The level of evidence for BoNT differs with the anatomical location of therapy and several other variables. BoNT can be used as a single modality for focal spasticity or with multisegmental management for specific areas of spasticity.[2] BoNT should be offered as a treatment option to reduce muscle tone and improve passive function in adults with spasticity (Level A by the AAN's criteria), and should be considered to improve active function (Level B). One study found no change in clinical measurements of spasticity or ankle stiffness with BoNT-A. Other lower-level studies found improvement in ratings of spasticity.[20] Parents have reported a preference for intramuscular (IM) injections of BoNT over serial casting. There is a report of lower incidence of complications for botulinum toxin injections compared to casting.[59] In a multicenter open label clinical trial BoNT injections were given approximately every 3 months to children with CP. There was an improvement of dynamic gait pattern on the Physician Rating Scale (PRS) in 46% of patients at first follow-up. The mean duration of BoNT-A exposure was 1.46 years per patient and the response was maintained in 41–58% of patients for 2 years. A considerable number of patients discontinued therapy for various reasons. However about 75% of patients achieve their treatment goals following the initial injection sessions.[57] For patients with spastic CP and adult spasticity the benefit for BoNT treatment was maintained or enhanced for 4-6 treatments rounds.[60] For localized/segmental spasticity in upper and lower extremities that needs treatment, BoNT-A should be offered (Level A evidence by the AAN's criteria).[7] There is growing evidence that BoNT-A is effective in reducing spasticity and improving function in the upper and lower limbs for children with CP.[61]

Table E-2. Framework A: Spasticity (continued)

Issue	Examples
Variations in interventions (continued)	The evidence for BoNT-A for improving function in CP is weak but the review suggests it is safe in the short term.[55] The use of BoNT with other treatment options can achieve functional benefit for CP, but there is insufficient evidence to support or refute the use of interventions after BoNT injections.[62] Use of BoNT-A in children with CP should never be considered a stand-alone treatment but should be combined with conservative and surgical strategies. However, there is insufficient evidence to either support or refute the use of these interventions before or after BoNT-A injections.[57] Using the PRS of gait as the primary outcome measure for meta-analysis there was improvement for BoNT-A compared to placebo (25% more of the treated group had a treatment "success" compared to the placebo group in a 3-trial meta-analysis) or compared to casting (23% more of the treated group had a treatment "success" compared to the casting group in a 2-trial meta-analysis). These effects were dosage-dependent. Treatment "success" was determined a priori to be a 2-point improvement in the PRS.[59] *Intramuscular Botulinum Toxin in Upper extremities.* BoNT-A has good level evidence to support therapeutic use for upper limb spasticity in children with CP. It should be used in conjunction with occupational therapy (OT).[63] Primary criterion for consideration of BoNT-A is hypertonia in absence of significant fixed deformity. In upper limbs, indications include persistent thumb in palm or thumb adduction; wrist posture preventing hand use, or tight elbow flexion.[11] A combination of BoNT-A and OT is more effective than OT alone in reducing impairment, improving activity level outcomes and goal achievement. When compared with placebo or no treatment, there is moderate evidence that BoNT-A alone is not effective. This systematic review found high level evidence supporting the use of BoNT-A as an adjunct to managing the upper limb in children with spastic CP. BoNT-A should not be used in isolation but should be accompanied by planned OT.[15] There is insufficient evidence on whether BoNT-A injection has any benefit on the spasticity or ROM of the upper limbs of children with CP.[64] The optimal age of injection, selection of target muscles, dose and dilution of volume of toxin, the ability to correctly identify target muscle, and methods of pre-treatment for pain/anxiety are factors that are not known for the use of BoNT-A in the upper limbs.[64] A systematic review found high level evidence to support the use of BoNT-A as an adjunct to OT in managing spasticity in the upper limb in children with spastic CP. When compared with placebo or no treatment, there is moderate evidence that BoNT-A alone is not effective. It is recommended that intramuscular injection of BoNT-A in the upper limb be administered using muscle localization methods.[15] Upper limb high muscle tone can be temporarily reduced following BoNT-A injection, with possible improved functional outcome. Most favorable response possibly in those children with at least moderately high muscle tone without fixed contracture, preserved grip strength, some distal voluntary control, intact sensation, and motivation to participate in post-injection training.[65]

Table E-2. Framework A: Spasticity (continued)

Issue	Examples
Variations in interventions (continued)	*Intramuscular Botulinum Toxin in Lower extremities*. Primary criterion for considering BoNT-A is either persistent or dynamic hypertonia in absence of significant fixed deformity. In the lower extremities, indications include dynamic equinus persistent through gait cycle, dynamic knee flexion angle greater than 20 degrees during gait cycle/interfering with gait, or significant scissoring or adduction at hips.[11] BoNT is relatively ineffective for treating hamstring contractures in larger children and adolescents.[8] A systematic review of BoNT-A in the treatment of lower limb spasticity in children with CP was performed by searching the Movement Disorders Review Group trials register, the Cochrane Controlled Trials Register, MEDLINE, pharmaceutical company databases, communication with other researchers in the field, and the reference lists of trials identified. There were only three RCTs identified. One compared BoNT vs. placebo in 12 patients. There was improvement with BoNT treatment that was not statistically significant. Two other studies compared BoNT-A vs. cast. There was no statistically significant difference between these groups. There were improvements from baseline in gait, range of ankle movement, and muscle tone in both groups. Meta-analysis was not possible on these three studies. The review determined that evidence that BoNT-A injections improves function in CP is weak.[55] For lower extremities of children with CP, BoNT injections show dose-dependence and moderate treatment effects compared to placebo.[59] RCTs of initial BoNT treatment of pes equinus deformity show efficacy rates of 50 and 61%. Initial reports show that 75% of patients achieve treatment goals after initial injection, but many stop therapy for a variety of reasons.[62] There is insufficient evidence to support or refute the benefit of additional casting to BoNT injection of the gastrocnemius-soleus muscles (inconsistent Class II and III studies) and the injection of BoNT into the hamstrings (only Class IV studies). In patients with adductor spasticity, BoNT injection is probably effective in improving adductor spasticity and range of motion (one Class I study), as well as postoperative pain in children undergoing adductor muscle lengthening surgery (one Class I study). In patients with upper extremity symptoms, BoNT injection is probably effective in improving spasticity and range of motion (two Class II studies and one Class III study).[19] A previous systematic review concluded that the evidence was not strong enough to support or refute the use of botulinum toxin A for lower limb spasticity. For severely impaired children the evidence is equivocal for achieving functional improvements with BoNT-A injections, but less impaired children have shown some benefits. There is a low rate of major adverse events compared to SDR and intrathecal baclofen.[59] *Pharmacology and Dosing of Intramuscular Botulinum Toxin*. A single set of botulinum injections produced results in 1-3 days, peak after 4 weeks, provides benefit for 3-4 months, and may be repeated every 3-6 months.[6] Dosages of BoNT-A (Botox® and Dysport®) and BoNT-B (Myobloc®) must be calculated based on units per kilogram with limits on maximum total units. The calculations are different for each preparation and there are no fixed dose-conversion factors.62 A different review cited cross-study comparisons as having a relative dose equivalents of Botox®: Dysport®: Myobloc® of approximately 1:3 – 4:50 –100.[19]

Table E-2. Framework A: Spasticity (continued)

Issue	Examples
Variations in interventions (continued)	*Antibody Development for Intramuscular Botulinum Toxin*. There is typically a 3-4 months clinical response to BoNT injections for spasticity. Some patients are recommended to avoid injections more often than every 3 months to avoid antibody resistance.[7] Non-responsiveness to BoNT due to antibody development has been decreased by reformulation of BoNT preparations. This has resulted in an apparent decrease from the previously high level of antibody formation (up to 30%) in the 1990s.[62] Efficacy of BoNT-B in cervical dystonia suggests BoNT-B might be effective in treating patients with spasticity in spite of prior history of BoNT-A resistance.[14] Muscle Localization for Intramuscular Botulinum Toxin. Various techniques including ultrasound guidance and electromyography (EMG) are used for muscle localization at the time of injection but there is insufficient evidence to recommend an optimal technique.[15,19] ***Oral Anti-Spasticity Medications***. *Diazepam*. Diazepam in children often used as nighttime dose to aid sleep and decrease nighttime spasms. Studies show mild improvement in children with athetosis and spasticity.[12] For generalized spasticity that needs treatment, diazepam should be considered for short-term use (Level B evidence by the AAN's criteria).[7] *Dantrolene*. Dantrolene has been shown to be beneficial including improved active and passive range of motion when compared to placebo in studies that included children. Long-term use of dantrolene yielded greater levels of function than predicted prior to dantrolene administration. After long-term use of dantrolene older children had improved movement and maintained their highest level of function. In a different study 1.8% of subjects treated with dantrolene had evidence of hepatotoxicity.[12] Four trials showed dantrolene is more effective than placebo in children with CP, with improved range of motion. A combination of dantrolene and diazepam is better than the individual drugs. Athetoid CP also shows benefit in spasm, athetoid movement, and activities of daily living when treated with dantrolene.[12] There is insufficient data to support or refute the use of dantrolene (Level U evidence by the AAN's criteria).[7] *Oral Baclofen*. Compared to placebo, oral baclofen reduced tone and allowed both active and passive limb movement in children with CP.[12] However, according to Level U evidence by AAN's criteria, there is insufficient data to support or refute the use of oral baclofen.[7]

Table E-2. Framework A: Spasticity (continued)

Issue	Examples
Variations in interventions (continued)	*Tizanidine and Clonidine*. Tizanidine is reported to be similar to diazepam and baclofen in effectiveness of tone reduction although studies are primarily in adults.[8] For generalized spasticity that needs treatment, tizanidine has Level C evidence by the AAN's criteria.[7] There is insufficient evidence to assess tizanidine's effect on motor function.[7] The use of clonidine orally and intrathecally has shown benefit in adults for treatment of spasticity and neuropathic pain after spinal cord injury.[12] *Gabapentin*. Although there is some evidence in adults with spasticity from multiple sclerosis and spinal cord injury, there is no evidence available for children with CP.[12] ***Intrathecal Baclofen Therapy***. Intrathecal baclofen has been shown to reduce tone in patients with spasticity of cerebral and spinal origin, and has been shown in children and adults to reduce both leg and arm tone.[12,14] Spastic quadriplegia with well-preserved cognition is best treated with intrathecal baclofen.[1] There is insufficient data to support or refute the use of continuous intrathecal baclofen (Level U evidence by the AAN's criteria).[7] Randomized trials identified by a systematic review of the management of the lower limbs of children with CP were rated for methodological quality. There is grade B evidence by Sackett's evidence criteria for intrathecal baclofen.[59] Intrathecal baclofen reduced spasticity in lower extremities and improved ease of care but medical complications were common. Few outcomes were measured beyond muscle tone.[66] **Surgical Treatment Strategies**: It is not necessary for a child with severe spasticity to have failed oral anti-spasticity meds before being considered a surgical candidate.[1] ***Orthopedic Surgeries***. Orthopedic surgery should be reserved only for muscular contracture or impending joint dislocation. Orthopedic surgery is best for children 4-7 years old, especially soft-tissue releases.[10] Per consensus recommendations, spastic quadriparesis plus severe cognitive impairment is better served by orthopedic procedures alone, although they also respond well to intrathecal baclofen.[1] Combined neurosurgery and orthopedic management is optimal.[1]

Table E-2. Framework A: Spasticity (continued)

Issue	Examples
Variations in interventions (continued)	Randomized trials identified by a systematic review of the management of the lower limbs of children with CP were rated for methodological quality. The evidence for orthopedic surgery is grade C by Sackett's evidence criteria (no RCTs).[59] *Tendon Lengthening*. Tendon lengthening is the preferred method of managing soft-tissue manifestations of spasticity, as opposed to tenotomy or tendon release.[10] *Tendon transfers*. Tendon transfers should only be done by an experienced surgeon and are contraindicated in patients with athetosis.[10] *Osteotomy.* Osteotomy can be used with tendon lengthening or release to prevent hip dislocation and other skeletal deformities.[10] *Tendon Release*. Tendon releases are an excellent option in teenagers with moderate to severe contractures of the hamstrings and crouch gait, and it is likely that these patients will not require a repeat lengthening procedure since they are essentially finished growing.[8] *Arthrodesis*. Arthrodesis (joint fusion) is useful to stabilize joints with deformities that cannot be braced.[10] *Thumb-in-palm.* Of all surgical treatment in CP, the treatment of the thumb-in-palm has the most recurrences. There are a number of different operative techniques and there is no consensus on treatment for thumb-in-palm deformities. There are questions of influence of age, intelligence, and sensibility for overall result of operation.[67] Surgery for thumb-in-palm shows some benefit, though not dramatic. Selection criteria include some voluntary motor control and cognitive ability and motivation to rehabilitate.[67] *Hip disease.* Adductor muscle release with or without obturator neurectomy has been used for spastic hip disease. Posterior transfer of adductors is another treatment option. There has been no agreement as to which is best.[10] Therapies to treat hip subluxation include lengthening of muscles (e.g., adductor longus and gracilis, adductor brevis, iliopsoas, and proximal hamstrings). Additionally, anterior branch obturator neurectomy is added in nonambulatory children that are very spastic but is contraindicated in ambulatory children.[10]

Table E-2. Framework A: Spasticity (continued)

Issue	Examples
Variations in interventions (continued)	***Neurosurgical Interventions***. These surgeries include SDR and implantation of intrathecal baclofen pumps (discussed above). SDR has been shown to improve stride length and efficiency of gait and to halt progressive hip subluxation; has been reported to improve upper-extremity tone and swallowing.[9] Pure hemiplegic CP is better treated with a combination of intrathecal baclofen and orthopedic interventions instead of SDR.[1] Older children may not improve with a SDR as much as children under 6 years old. Orthopedic interventions can be done at any age if an anatomic structure is at risk, including SDR.[1] The greatest benefit for the SDR procedure occurs in 3-7 year-olds with spastic diplegia but stable trunk control and good lower extremity strength.[6] Children with spasticity in only one major muscle group who would also be able to have BoNT injections or chemical denervation should also consider selective peripheral neurotomy.[9] Randomized trials identified by a systematic review of the management of the lower limbs of children with CP were rated for methodological quality. According to Sackett's evidence criteria there is grade A evidence (more than 2 RCTs) for SDR compared to physiotherapy.[59] **Rehabilitative Treatment Strategies**: Physical management of spasticity requires different strategies depending on the age of the patient with CP. From 0 to 3 months old: Need OT with feeding evaluation, maybe physical therapy (PT) (especially with orthopedic issues), speech therapy only if severe oral motor deficit that may affect speech production. From 3 to 12 months old: OT if hemi- or quadriparetic, addressing fine motor development, feeding, activities of daily living, cognitive and sensory issues, PT for hemi-, di-, or quadriparetic. From 1 to 3 years: OT if hemi- or quadriparetic, sometimes diparetics for visual motor or oral motor issues, PT for hemi-, di-, or quadriparetics, speech treatment if quadriparetic and hemi- or diparetic only if diaphragm involved or significant oral motor, orthoses may be needed for hemi-, di, or quadriparetic. From 3 to 6 years old: OT may see diparetics for activities of daily living, also PT, speech, and orthotic treatment. From 6 to 12 years old: PT and OT usually at school with additional treatment for postsurgical care and skills not used in school; speech therapy usually school-based with extra help for additional assistive-devices; orthoses as needed. From 12 years old into adulthood: PT/OT may continue at school/outpatient as needed for post-operative, functional independence, or adaptive equipment; speech treatment may continue at school or with new communication equipment, and orthoses as needed.[13] *Physical Therapy*. PT is needed in the first 4 years of life. Orthotic support up to 4 years might interfere with motor development.[10]

Table E-2. Framework A: Spasticity (continued)

Issue	Examples
Variations in interventions (continued)	Randomized trials identified by a systematic review of the management of the lower limbs of children with CP were rated for methodological quality. By Sackett's evidence criteria there is grade A evidence (more than 2 RCTs) for physical therapy but it had an equivocal or small effect.[59] See Framework B (Gait and Physical Therapy). *Occupational Therapy.* Further work is required to establish what specific therapy will enhance functional outcomes and prolong the beneficial effects of BoNT-A: traditional OT interventions, including such elements as facilitation of movement or task training, in combination with BoNT-A, BoNT-A plus splinting, CIMT, or OT and electrical stimulation as biofeedback to weak antagonists.[65] See Framework C (Upper Extremity and Occupational Therapy). *Postural Management*. Individually-tailored postural management programs (may include special seating, night-time support, standing support, active exercise, orthoses, surgery, individual therapy) help children with bilateral CP to facilitate communication, cognitive and functional skills, and enhance participation. The aim is to increase comfort and may reduce deformity.[4] Children with GMFCS level III require postural management programs that emphasize postural activity from an early age.[4] Children in GMFCS groups IV-V should start 24-hour postural management programs in lying as soon as possible after birth, in sitting from 6 months, and in standing from 12 months.[4] *Serial Casting.* By Sackett's evidence criteria there is grade B evidence for serial casting (small RCTs).[59] There is no evidence that serial casting can prevent surgery.[10] *Passive Stretching*. There is some evidence to show decreased spasticity from passive stretching but this is not carried over into functional activities like walking. There is conflicting evidence on whether passive stretching can increase the range of motion in a joint. Passive stretching should be used as an adjunct and not a primary therapy.[68] *Orthoses*. Randomized trials identified by a systematic review of the management of the lower limbs of children with CP were rated for methodological quality. There is grade C evidence (Sackett's criteria) for orthoses.[59]

Table E-2. Framework A: Spasticity (continued)

Issue	Examples
Variations in interventions (continued)	*Strength Training*. Strength training does not increase spasticity or contractures for patients with CP. Studies report increases in strength, improvements in activity, and improvement in self-perception.[69] By Sackett's evidence criteria there is grade C evidence (no RCTs) for strengthening.[59] *Gait Analysis.* Gait analysis has been used before and after surgery in ambulatory patients.[1] **Non-Treatment Strategies**: Because spasticity can be functional, treatment of spasticity may not always be indicated.[7] **Prevention and Surveillance**: ***Imaging***. In some cases, imaging is necessary to follow the musculoskeletal changes that accompany spasticity. *Hip Radiographs*. It is recommend that children who cannot walk more than 10 steps by 30 months have a hip radiograph to measure migration percentage of each hip, and repeat every 6-12 months until age of 7 years or when further deformity is unlikely. If the migration percentage is more than 14% at 30 months, then postural management at night and ongoing radiological monitoring are recommended.[4] *Spine Radiographs.* Spine radiographs at 5 years and 10 years are recommended for GMFCS groups V and IV who are unable to stand by 5 years.[4] ***Medical Home and Follow-up Care***. There are variations in the specific types of specialist and subspecialist involved in longitudinal care. A primary care medical home should work with parents, medical specialists, and community agencies.[6] ***RehabilitationTherapy***. See above.
Variations in target outcomes	Variation in target outcomes includes differences like functional outcomes versus anatomical outcomes. Postural intervention can be guided by child's functioning on GMFCS.[4] Effectiveness of BoNT-A is evaluated by ability to produce reductions in muscle tone, strength of contractions, and improvement in muscle balance in targeted muscles/groups, as well as the functional gain of mobility, dexterity, energy expenditure during movement, or comfort.[11] Assessment can be performed with EMG, kinetic joint analysis, ROM at target joint, muscle lengthening assessment, muscle strength assessment, functional impairment measures (Ashworth Scale), and dexterity assessment.[11] Target outcomes can include improved range of motion, ease of movement, and comfort.[8] In a systematic review of the upper limb dysfunction included assessments of—upper limb function, self-care, and individualized outcomes: Melbourne Assessment of Unilateral Upper Limb Function; Erhardt Developmental Prehension Test; Pediatric Motor Activity Log—amount of use; Pediatric Motor Activity Log—quality of use; Emerging Behavior Scale; Jebsen, Jebsen Taylor Test of Hand Function; and the Assisting Hand Assessment.[17]
Variations in service delivery models	There are variations in the service delivery models. It is recommended that assessment, intervention, and management be integrated into the child's daily activities at home, school, etc.[3]

Table E-2. Framework A: Spasticity (continued)

Issue	Examples
Variations in management strategies	There are variations in management strategies. Management of hypertonicity in the patient with CP involves multiple approaches, including environmental manipulations such as reducing sleep deprivation, alleviating pain, therapeutic use of heat and/or deep tissue massage, and reducing prolonged periods of immobility. Multiple oral medications are used to treat spasticity but have limited efficacy in most patients due to unacceptable side effects. Oral medications to treat dystonia, such as levodopa, can improve motor function in patients with spastic quadriplegia or mixed athetoid/spastic forms of CP. Neurosurgical interventions include the baclofen pump and SDR. Placement of a pump to allow the delivery of baclofen directly to the spinal cord is more effective at reducing spasticity and dystonia without the cognitive side effects that are frequently seen with oral administration of the drug. SDR involves the selective ablation of dorsal nerve rootlets and results in reduced tone in the lower extremities.[8] Consensus recommends defining goals and using PT/OT with every age group. Also recommend are oral medications, especially in spastic quadriparesis.[3] Management options include physiotherapy, conductive education strengthening, orthoses, serial casting, phenol, botulinum toxin, electrical stimulation, intrathecal baclofen, SDR, and orthopedic surgery. Compared to some other interventions, BoNT-A may have more supportive evidence because it is more amenable to being studied in prospective randomized trials. Potentially harmful interventions like SDR and BoNT-A have tended to undergo more scientifically rigorous trials.[59] Recommendations for therapy include: functional therapies to support motor development in all children with CP; orthoses and other aids to improve function and prevent structural deformities; oral anti-spasticity medication to generally reduce muscle tone, must often be used short- or medium-term due to habituation and systemic side effects; BoNT-A can be used for GMFCS I-V; intrathecal baclofen recommended for GMFCS IV and V (rarely III) with monitoring at an experienced center to minimize adverse events; and orthopedic surgery, especially in GMFCS IV and V who need to have hip monitoring.[57]
Variations in clinical practice	See Variations in management strategies
Variations in provision of services	Organizations: None Professionals: Recommend early referrals to PT/OT/speech therapy, etc.[3] Specialty, Primary: Multidisciplinary setting with fellowship-trained pediatric subspecialists.[1-3,6,9] Furthermore, there is a recommendation that patients without easy access but with sustained sensorimotor challenges, and/or needs for specialized intervention (i.e. baclofen pump), and/or needs to be followed by two or more services be sent for baseline assessment and consultation with a pediatric multidisciplinary team. Other: Recommend database of children needing postural management for results of radiological surveillance, intervention, and assessments.[4] Private: None Public: None
Variations in treatment rates and availability of care	None

Table E-2. Framework A: Spasticity (continued)

Issue	Examples
Uncertainty/controversy regarding outcomes	Better outcome tools are needed for patients undergoing surgery for movement disorders related to CP, and should incorporate quality-of-life (QOL) measures.[1] There are multiple ways to measure spasticity, as seen in the Park systematic review where studies used the Ashworth Scale, Modified Ashworth Scale, wrist resonance frequency, and Tardieu method. ROM was also measured with active and passive measurements, web-space method, and Norkin and White procedure. Functional changes of upper limb assessed with Quality of Upper Extremity Skills Test (QUEST), Pediatric Evaluation of Disability Inventory (PEDI), and Melbourne Assessment.[64] Many studies of BoNT-A use the Physicians Rating Scale of gait (PRS) or closely related scales as the primary outcome measure.[59]
Uncertainty/controversy regarding outcomes (continued)	Except for tone, few outcomes are repeated across different trials of BoNT-A. Computerized gait analysis may be able to determine the quality of the gait in a reproducible way. The combination of the GMFM (Gross Motor Function Measure) and the GMPM (Gross Motor Performance Measure) may be an appropriate outcome measure for BoNT-A treatment in children.[55] There is insufficient evidence that uses body function or activity as outcomes to look at BoNT-A injections in the upper limb of children with CP. Studies are limited by the reliability and validity of muscle tone measurements (e.g., modified Ashworth Scale), the small size of experimental and control groups, or the absence of certain study outcomes such as improved upper limb function.[58]
Uncertainty/controversy regarding methodology	Long-term follow-up (10-20 years) of patients after SDR, intrathecal baclofen, or orthopedic intervention need to be reported to determine long-term efficacy, changes in quality of life, and side effects.[1] Consensus recommends long-term prospective natural history studies of children with spasticity due to CP.[1] Some authors also discuss if RCTs are better than single case study designs to analyze spasticity, considering that in this last method the patient is compared with himself, decreasing several sources of bias such as anosognosia, neglect, or other cognitive symptoms, which could interfere in the outcome. The problems just described are common in sequels of stroke, but rare in patients with spastic equinus foot and were not described in any patient of the series analyzed in the present work. As spastic equinus foot represents one of the most uniform groups of spastic patients, RCTs continue to be the main method to analyze the role of BONT-A in this group of patients.[21]
Uncertainty/controversy regarding concept	None
Uncertainty/controversy regarding diagnosis	Tools to measure spasticity are the Ashworth scale and Modified Ashworth scale, which measure neural and mask factors of non-velocity-dependent hypertonia in addition to spasticity. Delgado et al. prefer the Tardieu scale, which accounts for the joint angle measure of the spastic phenomenon at different velocities of joint movement.[7]

Table E-2. Framework A: Spasticity (continued)

Issue	Examples
Uncertainty/controversy regarding treatment	**Pharmacologic Treatment Strategies**: There is a need for large RCTs of oral anti-spasticity drugs to assess effects on spasticity, functional movements, and QOL.[70] *Intramuscular Botulinum Toxin.* There are uncertainties about the factors that determine continuation or discontinuation of BoNT therapy.[57] There is insufficient evidence to determine whether BoNT-A improves motor function (Level U evidence by the AAN's criteria).[7] There is insufficient data for use of intramuscular injections of phenol, alcohol, or botulinum type B (Level U evidence by the AAN's criteria).[7] Studies are needed to identify the children that are most likely to respond to BoNT-A injections, monitor longitudinal outcomes, determine timing and effect of repeated injections, and optimal dosage, dilution, and volume schedule.[61,63] Further work is required to establish what specific therapy will enhance functional outcomes and prolong the beneficial effects of BoNT-A: traditional OT interventions, including such elements as facilitation of movement or task training, in combination with BoNT-A, BoNT-A plus splinting, CIMT, or OT and electrical stimulation as biofeedback to weak antagonists.[65] *Intramuscular Botulinum Toxin in Upper extremities*. Studies of the use of BoNT-A injection for spastic upper limb management in children would benefit from standardization of assessment tools, dosing regimen, and localization.[64] Further studies are necessary to determine which children would be most likely to respond to upper limb BoNT-A injections (i.e., age, severity of spasticity, degree of intellectual impairment, sensory status, and amount of baseline selective motor control).[15] There is a question of what age responds best to BoNT-A injection and if there is a relationship between age and functional gain. There is also no data on which muscle groups are best for injection.[64] Further research is essential to identify children most likely to respond to BoNT-A injections, monitor longitudinal outcomes, determine timing and effect of repeated injections and the most effective dosage, dilution, and volume schedules. The most effective adjunct therapies, including frequency and intensity of delivery, also requires investigation.[15] *Intramuscular Botulinum Toxin in Lower extremities*. Further research is needed as to why people stop BoNT therapy.[62] There is insufficient evidence on casting with BoNT injection of the gastrocnemius-soleus muscles and the injection of BoNT into the hamstrings.[19] There is limited evidence for the use of BoNT-A for improvement of activities of daily living, positioning, and care.[59] *Pharmacology and Dosing of Intramuscular Botulinum Toxin*. There are uncertainties about dosing because the calculations are different for each preparation BoNT and there are no fixed dose-conversion factors for relative dose equivalents of Botox®, Dysport®, and Myobloc®.[62] Further studies are necessary to determine the impact of different types of BoNT-A, dosages, and the number of injections per muscle.[15] Longer-term studies are required to determine if outcomes are maintained with multiple BoNT-A injections.[15]

Table E-2. Framework A: Spasticity (continued)

Issue	Examples
Uncertainty/controversy regarding treatment (continued)	*Antibody Development for Intramuscular Botulinum Toxin*. The efficacy of BoNT-B after a history of BoNT-A resistance is uncertain.[14] Further studies are necessary to determine the factors that affect biological resistance and changes in muscle following repeated BoNT-A injection over time.[15] *Muscle Localization for Intramuscular Botulinum Toxin*. There is insufficient evidence to recommend an optimum technique for muscle localization at the time of injection (Level U).[19] Further studies are necessary to determine the efficacy of various muscle localization techniques when injecting BoNT-A.[15] ***Oral Anti-Spasticity Medications***. There is uncertainty about the efficacy of diazepam.[7] There is uncertainty about the efficacy of dantrolene.[7] There is uncertainty about the efficacy of oral baclofen.[7] There is uncertainty about the efficacy of tizanidine and clonidine.[7,12] There is no evidence available for the use of gabapentin in children with CP.[12] ***Intrathecal Baclofen Therapy***. There is uncertainty about the efficacy of continuous intrathecal baclofen.[7,59,66] **Surgical Treatment Strategies**: There is a need for a prospective RCT comparing efficacy of SDR, intrathecal baclofen, and orthopedic intervention in patients with spastic diplegia.[1] ***Orthopedic Surgeries***. There is a need for RCTs for orthopedic surgery.[59] ***Neurosurgical Interventions***. There is a question of whether SDR is better than intrathecal baclofen or orthopedic procedures, especially for children with ambulatory potential.[9] Replacement laminoplasty may reduce long-term pain and spinal instability and may be considered for children undergoing multilevel laminectomy for SDR; however, we need further prospective long-term outcome studies to see incidence of pain, spinal deformity, and spinal stenosis after multilevel laminectomy for SDR.[1] There are no studies for whether spastic diplegic patients are best treated with SDR or intrathecal baclofen. There is a need for a controlled trial of SDR to determine necessity and optimal mode of neurophysiologic monitoring intraoperatively.[1] SDR may reduce the need for subsequent orthopedic operations. SDR may benefit the upper extremity tone as well as lower.[14] **Rehabilitative Treatment Strategies**: There is no agreement about most useful PT modality, frequency/duration, age group benefited, whether PT can be effectively performed by non-professionals (caretakers), or whether PT should be extended into adulthood.[10] Randomized trials identified by a systematic review of the management of the lower limbs of children with CP were rated for methodological quality. By Sackett's evidence criteria there is grade A evidence (more than 2 RCTs) for physiotherapy, but it had an equivocal or small effect, grade B evidence for serial casting (small RCTs), grade C evidence (no RCTs) for strengthening, and grade C evidence for orthoses.[59] See Framework B (Gait and Physical Therapy). Further work is required to establish what specific therapy will enhance functional outcomes and prolong the beneficial effects of BoNT-A: traditional OT interventions, including such elements as facilitation of movement or task training, in

Table E-2. Framework A: Spasticity (continued)

Issue	Examples
Uncertainty/controversy regarding treatment (continued)	combination with BoNT-A, BoNT-A plus splinting, CIMT, or OT and electrical stimulation as biofeedback to weak antagonists.[65] See Framework C (Upper Extremity and Occupational Therapy). There is no evidence that serial casting can prevent surgery.[10] There is conflicting evidence on whether passive stretching can increase the range of motion in a joint.[68] Prospective studies evaluating utility of gait analysis before and after surgery in ambulatory patients are needed.[1] Non-Treatment Strategies: There is uncertainty regarding the differentiation of functional spasticity from spasticity that is non-functional.[7] Prevention and Surveillance: There are uncertainties about the specific types and timing of involving specialist and subspecialists.[6]
Uncertainty/controversy regarding payor issues	There are no comparative studies of cost effectiveness and outcome of orthopedic releases vs. intrathecal baclofen in spastic quadriparesis plus severe cognitive impairment.[1] Economic evaluations of new therapies (e.g., BoNT) are rarely reported. This is a limiting factor for comparing treatment strategies.[59,61] An economic analysis is necessary to determine if BoNT-A injections are cost effective when compared to other interventions.[15]
Uncertainty/controversy regarding other issues	The efficacy and safety of medications for spasticity in children with CP need to be determined, including BoNT-A, BoNT-B, phenol, alcohol, oral baclofen, continuous intrathecal baclofen; should also study medications that have shown antispasticity in adults such as gabapentin.[7]
Emerging interventions	Intrathecal baclofen, with BoNT or tendon releases of spastic limbs, may ultimately be the treatment of choice for spastic hemiparetic CP.[9] Gabapentin has been used for multiple sclerosis, hemifacial spasm, and spinal cord injury in adults with improvement in spasticity. There is no report of studies that have been done on children.[12] Studies on the effects of weight training in patients with CP reported increases in strength, improvements in activity, improvement in self-perception; no adverse effects were reported.[69] Neurodevelopmental treatment (NDT) is a method of having efficient safe movement patterns against gravity, emphasizing sensation of movement, repetition, and sequential development of motor control. Therapeutic touch is also used, with treatment with movement, treatment with proprioceptive input, etc. There are a number of approaches that include different combinations of active and sensory techniques.[13]
Emerging approaches to management	None
Indication of a paradigm shift in diagnosis	None
Indication of a paradigm shift in treatment	None
Indication of a paradigm shift in management	None
Indication of a paradigm shift in understanding of CP	None

Framework B: Gait and Physical Therapy

One of the many complications of CP is gait dysfunction (Table E-3). Walking difficulty can be caused by spasticity, reduced lower extremity (LE) strength, decreased muscle coordination, and structural problems. A variety of interventions have been attempted to decrease the disability associated with lower extremity impairments in people with CP.

The primary types of therapies investigated to aid gait and LE function include orthoses,[22,24] body weight supported treadmill therapy (BWSTT) and partial body weight supported treadmill therapy (PBWSTT),[71] static weight bearing,[71] BoNT-A with or without casting,[19-21,72] selective dorsal rhizotomy (SDR),[73] adaptive seating,[22] balance training protocols and devices,[22] Lycra garments,[22]progressive resistance exercises (PRE),[74] and aerobic exercises.[21,75-78] These therapies have been investigated with variable qualities of evidence, but there is no consensus for optimal treatment or combination of treatments for CP.

Although there are few practice guidelines for treatment of gait and LE dysfunction in CP, the existing guidelines recommend increasing functional mobility by individualizing the frequency and intensity of physical therapy based on age, ability, and post-op course.[79,80] According to the guidelines, sessions should also incorporate active participation of the patient to attain functional goals.[80] Physical therapists are encouraged to use direct resistive exercises in 2-3 weekly sessions for 6-10 weeks at 65 percent of maximum isometric strength or 3-10 repetitions maximum.[79,80] Guidelines for physical therapists indicate that assistive technologies such as orthoses, wheelchairs, walkers, or crutches may be effective, as well as other strengthening exercises including electrical stimulation, bike riding, aquatics, and hippotherapy.[79,80] Guidelines recommend that certain programs should not be used; including an exercise program comprised primarily of passive stretching delivered by a therapist (parents or patients can be instructed to carry out these exercises themselves). Passive-reflexive (massage) techniques are deemed unnecessary. Therapeutic Electrical Stimulation (TES) to increase function has not been shown to be helpful. Classical neurodevelopmental therapy (NDT) where the emphasis is on "normalization" of muscle tone through passive handling techniques such as the use of reflex inhibiting patterns is also not recommended.[80] Finally, there are interventions that are still in development and should remain in development for the current time, including PBWSTT, robotic-assisted walking, and night splinting.[80]

Target outcomes are difficult to standardize for research on CP therapies. This is a common challenge to the synthesis of CP research. Recommended outcome measures of a variety of interventions include Tardieu, Ashworth, Gross Motor Functional Measure, or Gross Motor Performance Measure scales, ROM measurements, video recording of gait and movements, functional abilities such as walking, jumping, running, gait efficiency, gait velocity, gait cadence, gait kinetics and kinematics, endurance, strength, cardiovascular function, self-perceptions, self-worth, subjective well-being, ICF outcomes, and quality of life.[5,11,20,75,76,81]

Table E-3. Framework B: Gait and physical therapy

Issue	Examples
Availability of a strategy to reduce burden-Treatment	Therapies include orthoses,[22,24] BWSTT and PBWSTT,[71] static weight bearing,[71] BoNT-A with or without casting,[19-21,] 72 SDR,[73] adaptive seating,[22] balance training protocols and devices,[22] Lycra garments,[22] PRE,[74] and aerobic exercises.[21,75-78]
Availability of a strategy to reduce burden-Prevention	None
Variations in prevalence among individuals with CP	None
Variations in issues of diagnosis	None
Variations in age distributions	None
Variations in sociodemographic measures	None
Variations in interventions	There is variation in the types of physical therapy and physiotherapy used to improve gait and balance.[24,71,73,74,76-78,81-87] Variation in use of surgical and medicinal therapies to decrease spasticity and allow for improved gait.[19-21,72,73,78,88,89] The design and use of assistive devices including orthotics, specialized seats, special garments, etc. has great variability.[22,24,78,90] There is variability in the use of electrical stimulation protocols, which muscle groups are targeted, and use of functional electrical stimulation (FES) versus neuromuscular electrical stimulation (NMES).[91,92] Electrical stimulation has shown benefit in stroke patients, but studies in CP currently have very low evidence for electrical stimulation, to the point of not being a recommended therapy according to some investigators.[80, 91, 93] There is variation in the use of BoNT-A. Differences in practice include using casting instead of BoNT-A or as an adjunct with BoNT-A, targeting of various specific muscle groups, and doses used in different populations.[19-21,72,78,88]
Variations in target outcomes	There is variation in the outcome measures used to assess gait and functional abilities: Tardieu, Ashworth, GMFM, or GMPM scales, ROM measurements, gait and functional activities, participation in activities.[11, 20, 87] Current outcome measurements specifically for gait parameters include stride length, stride cadence, self-selected walking velocity, endurance, gait kinetics and kinematics, and computer gait analysis.[78, 83, 85, 89, 90] There is variation in the goals of physical therapy, including goals of increased strength, aerobic activity/cardiovascular function, as well as primarily gait-related parameters.[71, 74-77, 81,94]
Variations in service delivery models	None
Variations in management strategies	None

Table E-3. Framework B: Gait and physical therapy (continued)

Issue	Examples
Variations in clinical practice	There are significant variations in clinical practice. Variations include which populations require intervention, the timing of the onset of intervention, the type of interventions (i.e., medical, surgical, or physical therapy), the assessment of functional status at baseline, and the determination of the need for further intervention.
Variations in provision of services	Organizations: None Professionals: None Specialty, Primary: A multidisciplinary rehabilitation team is recommended.[5] Other: None Private: None Public: None
Variations in treatment rates and availability of care	None
Uncertainty/controversy regarding outcomes	There is uncertainty regarding appropriate instruments to measure short-term outcomes in physiotherapy. Questions also exist about the utility of video recording of gait and posture.[5] There is also uncertainty about the use of functional evaluation scales to evaluate outcomes such as walking, running, gait efficiency, self-perceptions, self-worth, self-confidence, and quality of life.[75,76] There is a need for international standards to assess long-term PT interventions.[81]
Uncertainty/controversy regarding outcomes (continued)	There is uncertainty regarding PBWSTT outcomes including the possible benefits: BMI improvement, growth, nutrition and bone health, neuroimaging changes, psychological impact, gait patterns, lower extremity muscle strength, functional walking independence, mobility-related self-care and community activities, walking speed, endurance, patient perception, and long-term gains.[84,85]
Uncertainty/controversy regarding methodology	None
Uncertainty/controversy regarding concept	None
Uncertainty/controversy regarding diagnosis	None

Table E-3. Framework B: Gait and physical therapy (continued)

Issue	Examples
Uncertainty/controversy regarding treatment	There is uncertainty about what type of PT would be best for each individual child with CP versus the population as a whole. The functional benefits of any of the interventions over the long-term are not known, especially the maintenance of effect and side effects. *Specific treatment uncertainties:* The optimal level of body weight support when using PBWSTT is not known, although research points toward 10-30% of body weight to have least gait distortion. Differences in baseline disability and IQ, progression of treadmill speed, percentage of weight support, facilitation of legs, and duration of treatment may confound results.[83,84] Furthermore, the effects of BWSTT on the onset of walking in young children are unknown.[83] The effects of different positions for static weight bearing exercises are uncertain.[71] The effects of PRE on functional abilities for people with CP are unknown. The possible long-term gains in motor function after discontinuation of therapy are also uncertain.[74] Isotonic strength training has shown positive trends for gaining and maintaining strength in children and adolescents with CP, but with similar challenges to the research to determine functional and long-term effects.[77] Different protocols for casting with and without BoNT-A make the process difficult to investigate.[20,88] Different treatment paradigms for use of orthotics in the literature can limit ability to determine efficacy. Also, limited data exists in the literature on the relationship of patient functional status and the evaluation of orthotics.[24,90] There is limited data on NDT and its effects on postural adjustment, very early treatment, severity of involvement, and other factors that might affect results of therapy. Follow-up has also been short.[86]
Uncertainty/controversy regarding payor issues	In one study, estimated additional cost of BoNT-A versus casting over a treatment interval of 3.7 years were $793 in children with hemiplegia and $867 for children with diplegia. However, BoNT-A was associated with four fewer hospital visits per year over the course of treatment.[72] The cost per exam for computerized gait assessment would be estimated $1800-2000 and would likely require multiple exams for full benefit.[89]
Uncertainty/controversy regarding other issues	None
Emerging interventions	Assistive devices to be used in CP are frequently being updated and redesigned, creating exciting new opportunities for improvements but also engendering difficulty with evidence-based assessment of the efficacy of new devices.[10] Computerized gait analysis may be useful to provide data on components of walking so that providers can plan surgery or other treatments more effectively. There is a need for evidence on whether the technology improves outcomes more than older diagnostic and treatment planning methods in order to justify cost.[89]
Emerging approaches to management	As more therapies become available, combination treatments are used more frequently clinically. This use of multiple therapies may create problems for researchers in determining the most effective interventions. Studies incorporating multiple treatments such as the research on BoNT-A and casting separately and then as a combined treatment may require investigation in the future.[19,72,78]
Indication of a paradigm shift in diagnosis	None
Indication of a paradigm shift in treatment	None
Indication of a paradigm shift in management	None

Table E-3. Framework B: Gait and physical therapy (continued)

Issue	Examples
Indication of a paradigm shift in understanding of CP	None

Framework C: Upper Extremity and Occupational Therapy

Patients with CP often have involvement of their upper extremities with impairments of spasticity, sensation, coordination, and strength (Table E-4). Spasticity, decreased strength, and structural problems can cause impairments in gross and fine motor function. There are few practice guidelines or consensus statements to shape clinical management of upper limb dysfunction.

Types of interventions for upper limb improvements include surgical, pharmacological, and rehabilitative therapies. Certain types of treatments are less commonly used due to lack of research evidence of efficacy or due to logistic difficulties of treatment. These treatments include hyperbaric oxygen, patterning motor treatment, and hippotherapy or horseback riding therapy.[6,95,96] Adaptive seating encompasses a wide range of seats of varying levels of complexity and has shown some benefit for patients. Individualized seating is recommended by at least one guideline, although posterior tilting is discouraged.[80,97,98] More commonly used therapies include casting or BoNT-A injections with or without occupational therapy (OT).[17,99-101] Wrist-hand orthoses have little evidence to back claims of efficacy, although they are widely used.[80] NDT and surgical therapy are two older types of intervention for upper limb dysfunction.[17,99,102] Emerging therapies include constraint-induced movement therapy (CIMT) and hand-arm bimanual intensive training (HABIT), different types of rehabilitative therapy to improve the use of the upper extremities.[17,53,80,81,103] CIMT may be especially useful in children with hemiplegia and mild to moderate impairments of manual dexterity.[80] Notably, there is no consensus on one therapy being remarkably better than any other therapy to improve outcomes for a particular patient.

Table E-4. Framework C: Upper extremity and occupational therapy

Issue	Examples
Availability of a strategy to reduce burden-Treatment	None
Availability of a strategy to reduce burden-Prevention	None
Variations in prevalence among individuals with CP	None
Variations in issues of diagnosis	None
Variations in age distributions	None
Variations in sociodemographic measures	None
Variations in interventions	There is variation in the use of OT, serial casting, BoNT-A, and NDT for increasing upper limb function.[17,99] The use of and efficacy of hippotherapy (therapy on top of a horse, performed with help from a licensed professional) and horseback riding therapy (HBRT, non-therapist riding instructors teaching according to child-specific needs) are not well defined.[6,95] There is significant variation in use and efficacy of adaptive seating for non-ambulant CP patients.[97]
Variations in target outcomes	There is variation in the target outcomes for adaptive seating for CP patients.[97]
Variations in service delivery models	None
Variations in management strategies	None
Variations in clinical practice	None
Variations in provision of services	Organizations: None Professionals: None Specialty, Primary: None Other: None Private: None Public: None

Table E-4. Framework C: Upper extremity and occupational therapy (continued)

Issue	Examples
Variations in treatment rates and availability of care	None
Uncertainty/controversy regarding outcomes	There is significant uncertainty about the most important outcomes of OT and whether OT programs meet desired goals. One systematic review of the efficacy of OT in children with CP determined that no conclusions could be drawn with the current data of the efficacy in increasing functional ability, social participation, QOL, and balance, or in decreasing muscle tone.[17, 101] The outcomes needed to determine efficacy of surgical interventions on hands and hand spasticity are not certain. Proposed outcomes include level of impairment and effect of intervention on activity, participation, and health-related quality of life, baseline stereognosis and cognition.[102] There are uncertainties regarding outcomes for adaptive seating in nonambulatory children and the effects of resultant changes in sitting posture or postural control on other aspects of functioning within the ICF.[98]
Uncertainty/controversy regarding methodology	There are known methodological standards for RCTs; however, a systematic review of the proportion of adequately reported PT/OT RCTs in children with CP found that only half of applicable items for each trial were reported adequately based on CONSORT statement.[104]
Uncertainty/controversy regarding concept	Uncertainty/controversy regarding the idea and utility of "developmental disregard" as a way to describe the learned non-use of one side of the body. Children with CP are unique in that they may have an early neurological insult and never have had capability or experience of using a limb normally. CIMT is supposed to overcome this barrier, although the impact of CIMT on undamaged brain regions during development and the possible impact of the stage of development during which CIMT is applied is unknown.[26, 103]
Uncertainty/controversy regarding diagnosis	None
Uncertainty/controversy regarding treatment	There is uncertainty and controversy regarding the use, benefits, and risks of hyperbaric oxygen therapy (HBOT) to improve functional outcomes for CP children. There is insufficient evidence of benefit, and adverse events include a higher rate of reported ear problems in CP patients than those reported in other brain injury/stroke. There is further uncertainty regarding the dosage and duration of treatment, relevant outcome measures such as caregiver burden, frequency and severity of adverse events.[105] There is uncertainty regarding the optimal use of CIMT. CIMT appears to improve the frequency and quality of use of the upper extremity for children with hemiplegic CP. Questions remain of length of time for casting the unaffected arm per day and overall duration of therapy needed for effective CIMT intervention.[17, 103] There is continued need for properly powered studies to verify efficacy.[17, 53] There are uncertainties regarding the effects of casting upper limbs of children or adults with spasticity from central nervous system (CNS) motor disorders. There is a need for adequate power, appropriate targets, clear participant inclusion criteria, consistent cast design, protocol, and safety management, and no-cast conditions for control in the studies. There is also a need to measure intensity of stretch provided by cast on the joint by determining the position of the joint in the cast.[100] The efficacy of surgical techniques for management of upper limb dysfunction in CP children is uncertain due to lack of high-level evidence.[99] Possible benefits, however, include hand mobility, strength, and functionality.[99,102] The efficacy of adaptive seating is uncertain. No intervention has currently been shown to be better than any other. There is no consensus as to whether improved posture would lead to improved functional abilities.[97, 98] Results from studies on populations with spinal cord injury and neural tube defect suggest that a posterior seat tilt of 20 or more reduces pressures under the pelvis. There is an overall lack of quality evidence to support and guide the use of the tilted position in seating for CP.[97]

Table E-4. Framework C: Upper extremity and occupational therapy (continued)

Issue	Examples
Uncertainty/controversy regarding payor issues	None
Uncertainty/controversy regarding other issues	None
Emerging interventions	CIMT is the repetitive training of affected limb in hemiplegia by forcing the affected limb to work and constraining the non-affected limb.[26, 103, 106] HABIT is a new type of physical therapy.[17] Additional RCTs required with adequate power and outcomes measurements for both interventions.[17] HBOT has inadequate evidence for significant benefit or for potential adverse effects when used in treating children with CP. Good evidence exists that HBOT is not different from pressurized room air for treatment of CP, and lower-level evidence exists that there are improvements in GMFM.[105]
Emerging approaches to management	None
Indication of a paradigm shift in diagnosis	None
Indication of a paradigm shift in treatment	None
Indication of a paradigm shift in management	None
Indication of a paradigm shift in understanding of CP	None

Framework D: Hip Disorders

Along with the high prevalence of gait dysfunction in individuals with CP, hips disorders are a common complication of CP (Table E-5). Typically, hip disorders include spastic subluxation, or dislocation, followed by surgery in some cases.[107] By 24 to 30 months old, the severity of motor disability becomes predictive of hip displacement, and individuals at the greatest risk for hip disorders are children with quadriplegic CP who cannot walk.[108] If untreated, the disorder can be a significant source of pain.[107]

Radiological measurement of migration percentage and acetabular index are techniques used to monitor hips that at risk for subluxation, but they are prone to error. [108] The reliability of the measurement increases as the child with CP grows, allowing continued monitoring after 8 years.[108] The hip is defined as subluxed if migration is between 33 and 80 percent and is defined as dislocated if migration is over 80 percent.[109] A systematic review of the evidence for hip surveillance in children with CP found that children who could walk 10 steps unaided by 30 months old did not need to undergo hip treatment by the age of 5.[108] The review also found that 4.1 percent of 5-year-olds who could walk 10 steps unaided and 46 percent of children who could not walk needed hip treatment.[108] Two studies found that surveillance programs eliminated the need for salvage surgery on dislocated hips.[108] One study found that for individuals involved in the surveillance program, preventative surgery increased and reconstructive and salvage surgery decreased, with preventative surgery undertaken at a significantly younger age compared with individuals in the conventional clinic.[110]

Children with CP should begin a postural management, or surveillance, program early in life before hip subluxation occurs.[109] A hip radiograph at 18 to 30 months old is recommended if hip adduction is pronounced, with repetition every 6 to 12 months until migration is stable.[108,109] At 30 months, if migration is >15 percent, positioning equipment should be used to control posture. A referral to an orthopedic surgeon is recommended at that time.[109] In addition to postural management, BoNT-A injections, orthoses, and sometimes surgery are required for a comprehensive treatment, although literature on the effectiveness of hip adductor surgery for dislocation/subluxation is preliminary.[107,109] Many factors determine the intensity and type of care each child receives. These factors include a child's functional status, pain levels, migration percentage, prognosis, and social-emotional implications.[109] Because treatment plans are so individualized to the child, studies profiling children for the purpose of choosing an appropriate intervention may be valuable in addition to RCTs.[109] There are no commonly-used practice guidelines for treatment of scoliosis or hip disorders for CP patients.

Table E-5. Framework D: Hip disorders

Issue	Examples
Availability of a strategy to reduce burden-Treatment	There are recommendations for all children with bilateral CP to have hip radiograph at 30 months or with clinical suspicion beforehand. Migration percentage should be used as most reliable index, with children with migration >33% or acetabular index >30 degrees, likely to need further treatment. Also, progression of percentage by more than 7% per year requires monitoring and possible orthopedic consult.[108] Children who are unable to sit unsupported at any time or walk more than a few paces with the use of aids (GMFCS groups IV-V) should start 24-hour postural management programs in lying as soon as appropriate after birth before hip subluxation occurs, in sitting from 6 months, and in standing from 12 months. All children who cannot walk more than 10 steps by the age of 30 months should have a hip radiograph to record the percentage of migration. If hip adduction is pronounced, a radiograph at 18 months may be helpful. Repeat radiographs are recommended every 6-12 months until hip migration is stable.[109]
Availability of a strategy to reduce burden-Prevention	Two studies of surveillance programs for hips eliminated the need for salvage surgery on dislocated hips. Researchers used migration % and acetabular index to identify hips with progressive subluxation. In the study of Dobson et al, the rate of preventative surgery was 70.9% after surveillance compared with 51% beforehand, whereas the rate of reconstructive and salvage surgery fell from 37.1% and 29% to 11.4% and 0%, respectively. Surgery was undertaken at a significantly younger age (mean 4.2 years) compared with that in the conventional clinic (mean 8.3 years). In one study, 54 of 78 hips (50 children) with a migration percentage greater than 33% required surgery, but in 18 hips it corrected to less than 33% without operation.[111] No hip with a migration percentage greater than 42% became normal without operation. All hips with an acetabular angle above 30° had a migration percentage greater than 33%.[108,110,111]
Variations in prevalence among individuals with CP	Children with quadriplegic CP who cannot walk have the greatest risk of hip displacement. In a district in the UK, 52% of children with quadriplegic CP required treatment for a hip problem by 5 years old compared with 21% with diplegia.[108] Hip dislocation occurs in 10-59% of patients by 7-8 years old. Untreated, hip dislocation is a significant source of pain and disability in approximately 50% of patients.[107]
Variations in issues of diagnosis	No child who had walked 10 steps alone by 30 months needed treatment of hips by 5 years old. 4.1% of children at 5 years old who could walk 10 steps unaided needed hip treatment, whereas 46% of children who were unable to walk needed hip treatment.[108] Radiological measurement of migration percentage and acetabular index can monitor hips at risk of subluxation. Children at highest risk are those with dislocated hips. In one study, the migration percentage of children without surgery who were unable to walk was 7.7%.[108] Hips were defined as subluxed if migration between 33-80% and dislocated if over 80%.[109]
Variations in age distributions	Severity of motor disability at 18 months was not predictive of hip displacement, but by 24-30 months, it was predictive.[108]

Table E-5. Framework D: hip disorders (continued)

Issue	Examples
Variations in sociodemographic measures	None
Variations in interventions	If hip migration is greater than 15% at 30 months, positioning equipment to control posture and referral to an orthopedic surgeon is recommended. Attempts to prevent hip problems should include postural management, botulinum toxin injections, orthoses, and surgery. The intervention chosen should take into account the child's clinical and functional status, pain levels, sleep assessment, percentage of hip migration, and long term prognosis, together with the implications of these in social and emotional terms. Training in postural care should be given to all people directly involved with the child: health professionals, parents, wheelchair services, education services, and respite carers.[109] Adductor releases for prevention of spastic hip subluxation and dislocation were studied in isolation or combined with other soft-tissue surgery around hip, such as psoas or hamstring release. Bony surgery was excluded. Radiographic hip subluxation was improved in 168 out of 530 hips after hip adductor release, with a corresponding improvement in Reimer's migration percentage in 241 of 467 hips. However, these results were weakened by the heterogeneity of the patient populations studied and the variability of the surgical procedures undertaken.[107]
Variations in target outcomes	None
Variations in service delivery models	None
Variations in management strategies	None
Variations in clinical practice	None
Variations in provision of services	None
Variations in treatment rates and availability of care	None
Uncertainty/controversy regarding outcomes	None
Uncertainty/controversy regarding methodology	Studies that profile children to determine the most appropriate interventions to reduce incidence of hip dislocation may provide more valuable information than RCTs.[109]
Uncertainty/controversy regarding concept	None
Uncertainty/controversy regarding diagnosis	Measurement of acetabular index to determine hip displacement risk is prone to error. Reliability decreases with size of femoral head and increasing age over 8 years. The reliability of migration percentage improves with growth, allowing continued monitoring after 8 years.[108]
Uncertainty/controversy regarding treatment	Evidence for postural management is limited and further research is needed.[109] There are substantial gaps in the body of evidence on hip adductor surgery to address dislocation/subluxation that need to be addressed by future research. Given the low frequency and variable severity of CP, multicenter studies are needed to recruit adequately matched samples. Not all subluxed hips progress to dislocation in children who have CP, so control groups must also be included, where ethically possible, to allow discrimination between the natural history of the condition and the effects of the intervention. Further studies to assess the reliability and validity of the available radiographic outcome measures are also required with correlation to criterion standard assessments of femoral head coverage, such as magnetic resonance imaging (MRI) and three-dimensional computerized-tomography (CT) imaging studies.[107]

Table E-5. Framework D: hip disorders (continued)

Issue	Examples
Uncertainty/controversy regarding payor issues	None
Uncertainty/controversy regarding other issues	None
Emerging interventions	None
Emerging approaches to management	None
Indication of a paradigm shift in diagnosis	None
Indication of a paradigm shift in treatment	None
Indication of a paradigm shift in management	None
Indication of a paradigm shift in understanding of CP	None

Framework E: Feeding and Nutrition Problems

Among the most distressing morbidities that may affect children and adults with CP are gastrointestinal and feeding-related disorders (Table E-6). Problems include drooling, constipation, inability to swallow, and possible nutritional deficiencies. Sialorrhea affects 10-37 percent of CP patients.[6,112] Prevalence rates of gastro esophageal reflux (GER) in children with neurological impairment (most commonly CP) range from 14-75 percent based on the diagnostic criteria used.[113] There are no commonly-used practice guidelines for feeding/nutrition issues for these patients.

Medical management of GER includes milk thickeners, H2-blockers, proton-pump inhibitors, antacids, and prokinetics. However, only 13 percent of neurologically impaired children are reported to respond completely to these interventions.[113]Surgical management of gastrointestinal disorders has been primarily used for swallowing dysfunctions and GER. Primary surgical interventions include gastrostomy tubes (Percutaneous endoscopic or open-insertion) and fundoplication, both of which are have possible benefits that are often mitigated by high surgical failure and post-op complications.[113-115] Medical management for drooling includes behavioral modification, oral motor stimulation therapy, botulinum-toxin injections, and medications such as glycopyrrolate, benztropine, and scopolamine.[6,112,116,117] Interventions for bone mineral density improvement that have been more well-researched include weight bearing activity, use of static or dynamic standing, vitamin D and calcium, oral or intravenous bisphosphonates, and growth hormone. Proposed interventions without significant research include vibrating platforms, vitamin K, and acupuncture.[118,119] It is notable that none of these have shown consistently significant results for CP children.[118]

Table E-6 Framework E: Feeding and nutrition problems

Issue	Examples
Availability of a strategy to reduce burden-Treatment	• Only 13% of neurologically impaired children respond completely to medical management (milk thickeners, H2-blockers, antacids, prokinetics).[113] • Drooling is a problem for 10-37% of children with CP. Possible interventions include oral motor stimulation therapy, behavioral modification, medication such as glycopyrrolate, benztropine, and scopolamine, botulinum-toxin injections, oral appliances, or surgery.[6,112] Often these treatments have significant adverse effects, limiting their utility.[112]
Availability of a strategy to reduce burden-Prevention	None
Variations in prevalence among individuals with CP	• There is variation in prevalence rates of GER in children with neurological impairment (including CP) ranges from 14-75% depending on diagnostic criteria used.[113] An estimated 6000 children in UK have significant feeding-related health problems due to CP.[115] Eight percent of children with neurological impairment including CP in the UK were gastrostomy-fed.[113]
Variations in issues of diagnosis	• There is variation in the diagnosis of osteopenia, osteoporosis, or decreased bone mass in children with CP. Dual-energy X-ray absorptiometry (DEXA) is most commonly used, but other imaging modalities such as ultrasound and lab markers of bone turnover need to be studied to determine utility in CP population specifically.[119]
Variations in age distributions	None
Variations in sociodemographic measures	None
Variations in interventions	• There is variation in determining when to use surgical interventions for feeding and nutritional problems in children with CP. • There is variation in decision-making for surgeries based on rates of surgical failure (up to 40% for fundoplication, also high for gastrostomy) and post-operative complications (including mortality of 1-3%) with the possible benefits of increased weight, height, nutrition status, decreased aspiration and GER, and possible emotional/social benefits.[113] • Variation in assessment and description of children with CP prior to surgery is based on their baseline level of function.[114] • There is variation in clinical and theoretical interventions for increasing bone mineral density. Interventions included weight bearing activity, use of static or dynamic standing, vitamin D and calcium, oral or intravenous bisphosphonates, and growth hormone, vibrating platforms, vitamin K, and acupuncture.[118]
Variations in target outcomes	None
Variations in service delivery models	None
Variations in management strategies	• There is variation in choice of surgery versus pharmacologic management for GER.[115] • There is variation in treatments for sialorrhea, including anticholinergic drugs, surgery, radiation, positioning techniques, and BoNT-A injections into salivary glands.[112,116]

Table E-6 Framework E: Feeding and nutrition problems (continued)

Issue	Examples
Variations in clinical practice	None
Variations in provision of services	None
Variations in treatment rates and availability of care	None
Uncertainty/controversy regarding outcomes	• Uncertainty exists about the best types of studies for salivary losses and treatment. There is a paucity of validated outcome measures for sialorrhea treatment.[112] • There is uncertainty regarding relevant outcomes for gastrostomy placement.
Uncertainty/controversy regarding methodology	None
Uncertainty/controversy regarding concept	None
Uncertainty/controversy regarding diagnosis	None
Uncertainty/controversy regarding treatment	• The enteral commercial formulas and amount of nutrients required by patients are not well defined. The best way to incorporate those nutrients into a gastrostomy-diet is also uncertain.[114] • There is uncertainty regarding effective drug delivery after gastrostomy.[114] • The effects of tube feeding on secondary and associated conditions of CP are not known, especially those that continue into adulthood.[114] • There is uncertainty concerning possible links between nutrient deficiency and osteopenia independent of the effects of associated anticonvulsant medications and immobility.[114] • Uncertainty of efficacy of use of anti-reflux medications versus fundoplication to treat GER after gastrostomy.[113,114] • Uncertainty regarding efficacy of benztropine, glycopyrrolate, and scopolamine versus placebo for sialorrhea.[112,117] • The efficacy of BoNT-A, propranolol, and metoprolol, as well as antireflux medications for treatment of sialorrhea is unknown.[112,117] • The maximum dose, location, and number of BoNT-A injections required into salivary glands to gain greatest efficacy for sialorrhea is not well characterized.[117]
Uncertainty/controversy regarding payor issues	None
Uncertainty/controversy regarding other issues	None
Emerging interventions	None
Emerging approaches to management	None
Indication of a paradigm shift in diagnosis	None
Indication of a paradigm shift in treatment	None

Table E-6 Framework E: Feeding and nutrition problems (continued)

Issue	Examples
Indication of a paradigm shift in management	None
Indication of a paradigm shift in understanding of CP	None

Framework F: Pain

Clinicians, researchers, families, and patients are well aware that pain can be a serious problem in CP (Table E-7). However, only a handful of papers on pain prevalence and very few on treatment of pain in CP have been published. Furthermore, no guidelines exist to address pain specifically in CP patients. The reported prevalence of pain in CP varies with over 50 percent of youth (8 to 20 years old) with developmental disabilities (predominantly CP) reporting pain during PT or OT or home therapy, 64 percent of a sample of CP children reporting pain as a problem, and 67 percent of parents reporting pain behaviors in their children with CP over the course of a month.[120,121] In adults with CP, 28 percent report chronic pain versus 15 percent of adults in the general population.[122]

Assessment of pain in patients with communication difficulties or cognitive impairment complicates both treatment and research.[6] Pain management in CP has not been studied broadly, although some of the research in children in general may be applicable to the CP population. In studies of children with CP that are getting PT interventions, the therapist's behavior and allowing time for patients to adjust to interventions can reduce distress from pain.[120] Data from typically developing children suggests that cognitive behavioral methods may be helpful as well, especially for acute pain, abdominal pain, and chronic headaches.[120]

Table E-7. Framework F: Pain

Issue	Examples
Availability of a strategy to reduce burden-Treatment	Strategies to address pain include medication, relaxation, biofeedback, cognitive-behavioral therapy, training in coping skills, hypnosis, exercise, distraction, and imagery.[120]
Availability of a strategy to reduce burden-Prevention	None
Variations in prevalence among individuals with CP	Fifty-eight percent of youth ages 8 to 20 years old with developmental disabilities reported pain during PT or OT, and 53% reported pain during a therapeutic home program.[120] Reports of pain most commonly associated with PT interventions of stretching and bracing.[120]
Variations in issues of diagnosis	Variations in expression of pain by patients make assessment challenging, especially when a patient has communication difficulties or cognitive impairment.[6] Variations in diagnosis of pain may be aided by possible pain assessment tools including self-report, physiological pain, behavioral pain, and distress measures.[120]
Variations in age distributions	None
Variations in sociodemographic measures	None
Variations in interventions	None
Variations in target outcomes	None
Variations in service delivery models	None
Variations in management strategies	None
Variations in clinical practice	None
Variations in provision of services	None
Variations in treatment rates and availability of care	None
Uncertainty/controversy regarding outcomes	None
Uncertainty/controversy regarding methodology	There is uncertainty regarding how to assess pain during PT therapy. There is a need for a reliable, valid tool to use in PT practice.[120] Caregivers' and physical therapists' perceptions of pain for children with CP are not well defined. There is uncertainty regarding characteristics, experiences, or beliefs of physical therapists that may influence the awareness of and responses to pain in children with CP. These uncertainties also include the psychometric properties of pain assessment tools used for children with CP.[120]
Uncertainty/controversy regarding concept	None

Table E-7. Framework F: Pain (continued)

Issue	Examples
Uncertainty/controversy regarding diagnosis	None
Uncertainty/controversy regarding treatment	None
Uncertainty/controversy regarding payor issues	None
Uncertainty/controversy regarding other issues	None
Emerging interventions	None
Emerging approaches to management	None
Indication of a paradigm shift in diagnosis	None
Indication of a paradigm shift in treatment	None
Indication of a paradigm shift in management	None
Indication of a paradigm shift in understanding of CP	None

Framework G: Other—Cognition, Seizures, Audiology, Optometry/Ophthalmology, Brain Imaging, etc.

Cognition

Although approximately 50 percent of patients with CP have some degree of intellectual disability, there is no standard guidance for how to assess cognition in these patients (Table E-8).[6,123] The incidence of cognitive impairment varies based on the subtype of CP, with the highest rate among individuals with spastic quadriparesis.[123] Conductive education therapy targets cognition and motor skills, but limited information is available to guide practice because there are no standard characteristics of the program, definite parameters, or baseline skill level for the study population.[124]

Communication is a multi-faceted problem for those with CP. Even in infancy, individuals with CP interact less with parents than typically developing individuals.[125] As the children age, problems with speech and other forms of communication can further complicate communication. Communication and speech/language therapy often involves teaching signals (non-verbal and verbal) as a main communication skill, although there is uncertainty about its effectiveness in facilitating independent communication in children with CP.[125] A Cochrane review on the effectiveness of speech/language therapy specifically for children with CP showed no significant evidence to support effectiveness.[126] Further research is needed on how to tailor speech/language and communication therapies for the CP population.[125]

Seizures

There is significant variation in the estimates of prevalence of seizures in children with CP (Table E-8). Seizures occur in anywhere from 16 to 50 percent of patients with CP.[6,56] Epilepsy is associated with increased intellectual disability.[56]

Sensory

Sensory impairments can contribute to difficulties communicating and interfere with cognitive development (Table E-8). The auditory and visual systems are subject to the same developmental insults that cause CP, therefore referral and surveillance is necessary in these patients.[6] Children with CP have increased incidence of strabismus, amblyopia, nystagmus, optic atrophy, and significant refractive errors. [56]

Brain imaging

MRI, CT, and ultrasound imaging can help to characterize anatomic abnormalities in patients with CP (Table E-8). MRI abnormalities were found in 77 percent of children with CP, with etiologic association solely from MRI in 23 percent.[56] There is uncertainty about the need for neuroimaging in patients with CP as imaging may not be necessary for the clinical diagnosis.

Table E-8. Framework G: Other—cognition, seizures, audiology, optometry/ophthalmology, brain imaging, etc.

Issue	Examples
Availability of a strategy to reduce burden-Treatment	The strategies to address cognition in children with CP involve the development of communication abilities through speech and language therapy, education strategies, and assistive technologies.[124-126]
Availability of a strategy to reduce burden-Prevention	Children suspected of having CP should have audiologic and pediatric ophthalmologic consultation.[6]
Variations in prevalence among individuals with CP	Approximately 50% of patients with CP have intellectual disabilities.[6] Early reviews of CP give ranges of 50-70% of CP children with IQ 69 or below; however, rates vary based on level of impairment and subtype. Spastic quadriparesis is usually severely intellectually impaired, half of hemiparetic children have average IQs, and 18% have IQs over 100. Spastic diplegia motor and cognitive defects tend to correlate. In extrapyramidal CP, motor defects are worse than cognitive.[123] Infants with CP initiate less interactions with parents, are less responsive, and less independent than other children. Parents control interactions with verbal and physical directives.[125] The Western Australian Cerebral Palsy Register described 21.4% of children born 1980-1994 as non-verbal (unable to produce intelligible speech).[126] Seizures occur in more than 25% of CP patients, with greatest risk among spastic quadriplegia and hemiplegia.[6] Epilepsy was found in over 50% of CP patients, with seizure onset usually less than 4 years after diagnosis. Epilepsy is associated with increased intellectual disability. There may also be electroencephalography (EEG) findings without clinical signs.[56] 16-27% of children with spastic diplegia will have seizures.[56]
Variations in issues of diagnosis	Optometric exams of children with CP and average intelligence (standard IQ between 85-115) have shown increased incidence of strabismus, amblyopia, nystagmus, optic atrophy, and significant refractive errors.[56] MRI abnormalities were found in 77% of children with CP, with etiologic association solely from MRI in 23% and supporting suspected etiology in 32%. Only 17% of children with minor motor delay had abnormal scans.[56]
Variations in age distributions	None
Variations in sociodemographic measures	None

Table E-8. Framework G: Other—cognition, seizures, audiology, optometry/ophthalmology, brain imaging, etc. (continued)

Issue	Examples
Variations in interventions	Possible solutions to communication problems include consistent, readable non-verbal and vocal signals that parents can recognize and respond to. However, the routine signals may make it difficult for the child to acquire a full range of communication skills and take an active independent role in interaction.[125] There is little information about neuropsychology-based testing of cognitive function in children with CP. The few available studies indicate possible utility for assessing baseline and change over time. For example, demonstrating improvement in different attentional and cognitive functioning following SDR.[123] Common features of conductive education (CE): (1) group work using a highly structured framework; (2) the use of a task series; (3) the use of rhythmical intention; and (4) the use of specific equipment. CE has multiple permutations in different countries.[124]
Variations in target outcomes	• Often there is a split between verbal IQ and performance IQ on Wechsler intelligence tests. In studies, after 2 years of school, verbal IQs increased significantly but performance IQs did not change, increasing the verbal-performance split. Verbal IQ of children in standard classrooms increased more than those of children in special classes, but performance IQ increase was greater for children in special classes. The manifestation of poorer functioning can also be associated with right-sided versus left-sided hemiplegia.[123]
Variations in service delivery models	None
Variations in management strategies	None
Variations in clinical practice	None
Variations in provision of services	None
Variations in treatment rates and availability of care	None
Uncertainty/controversy regarding outcomes	None
Uncertainty/controversy regarding methodology	None
Uncertainty/controversy regarding concept	None
Uncertainty/controversy regarding diagnosis	• There is uncertainty about the need for neuroimaging in patients with CP. There is controversy on whether the ventricles are significantly larger in CP patients with cognitive impairment versus those without.[56] • Future studies should delineate the relationship of MRI and brain lesions and effects of lesions on early, middle, and late childhood neuropsychological functioning. Neuropsychological assessment should also be used to better characterize CP subtypes.[56]
Uncertainty/controversy regarding treatment	• Future research on communication training for CP partners should involve refining training for partners to its most effective and efficient components and methods of provision, mapping training components to client groups and ensuring that training offered meets clients' needs as they define them.[125]
Uncertainty/controversy regarding payor issues	None

Table E-8. Framework G: Other—cognition, seizures, audiology, optometry/ophthalmology, brain imaging, etc. (continued)

Issue	Examples
Uncertainty/controversy regarding other issues	• There has been controversy about whether baclofen causes increased, decreased, or no change in seizure activity.[12]
Emerging interventions	None
Emerging approaches to management	None
Indication of a paradigm shift in diagnosis	None
Indication of a paradigm shift in treatment	None
Indication of a paradigm shift in management	None
Indication of a paradigm shift in understanding of CP	None

Framework H: Overall—Quality of Life, Functional Independence, Transitions, etc.

The "Overall" category for CP treatment targets is intended to encompass many of the social, educational, psychological, and quality of life (QOL) issues related to CP that cross-cut domains of life and health (Table E-9). Examples of functional independence and achieving functional independence through transition from pediatric to adult care are of great importance to stakeholders from patients and families to health care providers.

A handful of papers have addressed transitions in the CP population specifically.[127-134] Basic recommendations from professional societies on transition planning for adolescents with special health care needs are rarely based on statistical evidence of efficacy; rather, they build on commonly accepted principles of transition. The 2002 consensus statement from the American Academy of Pediatrics, American Academy of Family Physicians, American College of Physicians—American Society of Internal Medicine, the most commonly cited policy statement, defined the successful transition in health care as: "to maximize lifelong functioning and potential through the provision of high-quality, developmentally appropriate health care services that continue uninterrupted as the individual moves from adolescence to adulthood. It is patient centered, and its cornerstones are flexibility, responsiveness, continuity, comprehensiveness, and coordination."[135]

The National Center for Medical Rehabilitation Research model assesses quality of life on the basis of the interplay between the individual's functional limitations, family assets/challenges, and resources available in society.[6]There are an estimated 400,000 adults with CP. Survival until the age of 30 years occurs in 95 percent of diplegic children and 75 percent of quadriplegic children, and overall survival of all children with CP until the age of 20 years is 90 percent. As these children with CP age, they encounter possible QOL challenges due to their underlying condition and other comorbidities. In a surveillance of CP in Europe, learning disability was present in 40 percent of individuals with CP, epilepsy in 33 percent, and severe visual impairment in 19 percent.[136]Strauss and colleagues found an excess rate of mortality in adults with CP, resulting from cancer, stroke, and heart disease. [137] This rate may be a result of a lack of surveillance and detection.[136]

Recommendations for improving the overall well-being of patients with CP include: physiotherapy/speech therapy should be intensive and begin early in life;[5] regular constipation protocols should be followed, including oral stool softeners, bowel stimulants, rectal suppositories, and occasional enemas; [6] OT should be performed in conjunction with BoNT in order to target improvement of activity levels and goal achievement, although overall QOL and self-competence levels do not differ from OT alone.[15] Although BoNT decreases spasticity, there is disagreement about whether or not it has an effect on overall function or QOL. Despite the speculation, BoNT is recommended as part of a program that aims to reduce disability and promote social rehabilitation; further longitudinal studies are encouraged to determine efficacy and safety.[21] BoNT has been associated with various adverse events, including pharyngitis, unspecific pain, falls, respiratory tract infection, bronchitis, vomiting, seizures, urinary incontinence, asthma, viral upper respiratory tract infection, generalized weakness, and constipation.[18,20] More guidance is needed, specifically in respect to quality of life issues, including social/emotional aspects of living with CP, and how quality of life is defined in the context of various transition points throughout the patient's life.

Table E-9. Framework H: Overall—quality of life, functional independence, transitions, etc.

Issue	Examples
Availability of a strategy to reduce burden-Treatment	Physiotherapy and speech therapy should begin as early as possible in life; it should be intensive (1 hour of therapy 4 times more per week) and continuous, at least in early life. Recommendation for home physiotherapy to be avoided.[5]
Availability of a strategy to reduce burden-Prevention	Patients need prompt referral to early intervention services (EIS) for children from birth to 3 years of age if there is a suspicion of CP. After 3 years, a child is eligible for special-education from a local educational agency.[6]
Variations in prevalence among individuals with CP	The GMFCS for patients with CP has the following distribution: Level I (32%), Level II (29%), Level III (8%), Level IV (15%), and Level V (16%). Learning disability was present in 40%, epilepsy in 33%, and severe visual impairment in 19% of the children."[57] There are an estimated 400,000 adults with CP. 95% of children with diplegia and 75% of children with quadriplegia survive until the age of 30 years. 90% of children with mild mental retardation and 65% of children with severe mental retardation survive until the age of 38 years. Overall survival of all children with CP until the age of 20 years is 90%.[136]
Variations in issues of diagnosis	There are reports of excess mortality in adults with CP from common diseases such as cancer, stroke, and ischemic heart disease. This may be a result of poor surveillance and a lack of early detection. A lack of periodic health care, including breast examinations and routine gynecologic care has also been reported.[136]
Variations in age distributions	None
Variations in sociodemographic measures	None
Variations in interventions	A combination of BoNT-A and OT is more effective than OT alone in reducing impairment, improving activity level outcomes and goal achievement, but not for improving quality of life or perceived self-competence.[15] The results of one analysis suggest that BoNT-A has a relatively good safety profile during the first months of use. Extrapolations to long-term use are not possible with the available data. It is possible that BoNT-A is related to pharyngitis, unspecific pain, falls, respiratory tract infection, bronchitis, vomit, seizures, urinary incontinence, asthma and viral upper respiratory tract infection.[18]
Variations in target outcomes	None
Variations in service delivery models	There is variation in recommendations for financial, estate, educational, vocational, guardianship planning as well as transition to adulthood issues for children and adolescents with CP.[6,8,138]
Variations in management strategies	There is variation in the management of constipation in children with CP. Regular protocols must be followed by many children, including oral stool softeners and bowel stimulants, rectal suppositories, and occasional enemas. Also possible to have neurogenic bladder dysfunction and may require urologic consultation.[6]
Variations in clinical practice	None
Variations in provision of services	Organizations: None Professionals: None Specialty, Primary: None Other: None Private: None Public: None

Table E-9. Framework H: Overall—quality of life, functional independence, transitions, etc. (continued)

Issue	Examples
Variations in treatment rates and availability of care	None
Uncertainty/controversy regarding outcomes	None
Uncertainty/controversy regarding methodology	The World Health Organization and National Center for Medical Rehabilitation Research models assess the severity of CP at the cellular, organ, or whole-person level. The National Center for Medical Rehabilitation Research model assesses QOL based on interplay between the individual's functional limitations, family's assets and challenges, and resources and limitations of the society in which the child is immersed.[6]
Uncertainty/controversy regarding concept	None
Uncertainty/controversy regarding diagnosis	None
Uncertainty/controversy regarding treatment	Although many studies have reported that BoNT-A decreases spasticity in several groups of patients there is controversy over whether there is associated improvement in function or QOL in these patients.[21] BoNT-A injection is always part of a program that aims at reducing disability and promoting social rehabilitation. The role of BoNT-A in modifying the long-term prognosis of motor disorders in children with CP is still subject to speculation and should be defined through prospective studies with long-term follow up.[21]
Uncertainty/controversy regarding payor issues	None
Uncertainty/controversy regarding other issues	None
Emerging interventions	None
Emerging approaches to management	None
Indication of a paradigm shift in diagnosis	None
Indication of a paradigm shift in treatment	None
Indication of a paradigm shift in management	None
Indication of a paradigm shift in understanding of CP	None

Emerging Technologies for Cerebral Palsy

Research in recent years has included a number of new technologies that may be of benefit to children and adults with CP. Several of these technologies were highlighted by stakeholders as possibly important or interesting to consider when thinking about CP care. Notably, few of the therapies have greater than case series evidence to support their use. A horizon scan of the available literature on select emerging therapies for CP revealed that few of the therapies are available or recommended for clinical use. The potential benefits and risks are not well characterized.

Stem Cells

Theoretical support exists for the use of embryonic or neural stem cells injected into the brains of CP patients from infants to adults. Studies injecting embryonic neural cells into affected areas of adults after ischemic stroke or into the basal ganglia of patients with Parkinson's disease have demonstrated no significant utility.[139] However, there is preliminary evidence, primarily from *in vitro* studies and rat studies that neonatal models of hypoxic-ischemic brain injury may improve with injection of genetically engineered stem cells.[140-142] This therapy remains experimental.

Robotics

Robotics have been used for several years to aid upper body mobility and dexterity for stroke rehabilitation.[143,144] The therapies and machines have been adapted for CP patients who suffer similar motor impairments. A major difference between these two patient groups is that CP patients were never able to perform certain movements, whereas stroke patients likely had previous use of their affected limbs. Robots have also been employed to assist with treadmill therapy and improve the functional tasks of standing and walking.[145-148] Only case studies have been published thus far on these robotic modalities.

Neuroplasticity

Neuroplasticity is the human brain's ability to remap and change through a variety of means, from experiencing the world to recovering from injury. Theories of neuroplasticity are currently being used to investigate the injuries and subsequent disabilities seen in CP, as well as to explain theoretical benefits of therapies that could preserve the brain's natural ability to adapt and recover from injury.[149,150] Other emerging technologies such as transcranial magnetic stimulation (TMS) have been used to map motor areas and to demonstrate beneficial effect of therapies that exploit neuroplasticity.[151]

Vibration Therapy

Whole body vibration is another therapy that was originally used to improve balance and gait in Parkinson's disease and stroke.[151] Its mechanism of action is unknown. Patients stand stationary or perform dynamic movements while on the vibration platform. One hypothesis posits that the vibration platforms are able to stimulate muscle spindles and alpha-motoneurons that initiate a muscle contraction.[152] There have been positive effects in bone mineral density

muscle strength, gross motor function, and spasticity with the use of vibration therapy in a small number of patients with CP.[152,153]

Virtual reality

One systematic review of virtual reality says that the use of virtual reality (either immersion or desktop versions) has conflicting evidence of positive effects on body structures and functions.[154] There is a moderate level of evidence that virtual reality does not positively impact activity and participation. There is a moderate level of evidence that virtual reality therapy positively impacts personal factors such as motivation, volition, and interest.

Appendix F. Outcomes from the In-Person Meeting

Participants

Stakeholders

Beth Ansel, Robert Baumann, Peter Blasco (by phone), Suzanne Bronheim, Janice Brunstrom-Hernandez, Anna Marie Champion, Daofen Chen, Diane Damiano, Brian Faux, Deborah Gaebler-Spira, Carrie Gray, Cynthia Frisina Gray, Ashley Hall, Deborah Hirtz, Laurens Holmes, Thomas Koinis, Eric Levey, Susan Lin, Lemmietta McNeilly, James Michels, Susan Miller, Michael Msall, Jeffrey Okamoto, Bob Palisano, Peter Rosenbaum, Carmen Sanchez, Rich Stevenson (by phone), Bonnie Strickland, Chris Thomson, Glenn Tringali, Nora Wells, Marshalyn Yeargin-Allsopp

AHRQ

Shilpa Amin, Karen Siegel, Stephanie Chang, Beth Collins-Sharp, Lia Hotchkiss, Supriya Janakiraman, Harvey Schwartz, Joanna Siegel, Scott Smith

Vanderbilt EPC

Dwayne Dove, Allison Glasser, Katie Jackson, Melissa McPheeters, Tyler Reimschisel

SRC-SET

Beth Church, Pam Curtis, Cathy Gordon, Kay Mattson, Susan Stearns

Eisenberg Center

(by phone): Trinka Schneider, Tom Workman

Rutgers DEcIDE Mental Health and Developmental Disabilities Consortium Investigators

(by phone): Terri Viggiano

Overview

The Issues Exploration Forum on Cerebral Palsy was held to identify and prioritize important areas of research. As the last meeting in the forum, a group of 32 diverse stakeholders including consumers, consumer advocates, payers, clinicians, researchers, and Federal partners were convened in Rockville, Maryland to refine and prioritize potential research topics for the AHRQ Effective Health Care (EHC) Program.

Meeting Objectives

The objectives of the meeting were:

- To review, discuss and generate potential topics for systematic review in the area of cerebral palsy.
- To prioritize potential research synthesis topics in the area of cerebral palsy.

- To identify additional research and methodological issues and needs related to cerebral palsy.

I. Welcome

Pam Curtis opened the meeting, welcomed the stakeholders to the Issues Exploration Forum on Cerebral Palsy.

Shilpa Amin welcomed the participants on behalf of the AHRQ Center for Outcomes and Evidence. She thanked the participants for their time and participation on the conference calls and extranet discussion. She provided an overview of AHRQ and its mission, as well as a brief history of the EHC Program and its major components—evidence synthesis, evidence generation, evidence needs identification, evidence translation, and dissemination. She noted that the EHC Program is exploring stakeholder engagement methods and the Issues Exploration Forum is one process for stakeholder engagement that aims to bring end users into the decision process. She reviewed the goals of the forum including (a) to take topics that the participants have recommended and develop a prioritized list for comparative effectiveness research with a focus on evidence synthesis, and (b) to remain mindful of the need for evidence generation in this area. Using the forum and the initial list of topics, AHRQ hopes that that the participants' discussion and relationships will be continued in the future through the extranet and research activities of the various components of the EHC Program, and wishes to develop a pattern of research planning and development that engages stakeholders at every step of the research process. Shilpa indicated a long-term goal of the EHC Program developing a prioritized research agenda in CP and developmental disabilities.

II. Introductions and Meeting Orientation

Stakeholders, AHRQ staff, Vanderbilt EPC staff, SRC staff, and other guests introduced themselves. Pam Curtis reviewed the meeting materials, logistics, announcements, and the process to date including results of the first two conference calls and extranet discussion board. The initial list of 88 research topic ideas generated from the conference calls and extranet discussion was presented for initial prioritization in the week prior to the meeting.

III. Review of the Evidence: Existing Guidelines, Consensus Statements and Meta-Analyses for CP related topics

Tyler Reimschisel presented a review of the information from the Vanderbilt Evidence-based Practice Center on existing guidelines, consensus statements, and meta-analyses including systematic reviews (see Appendix C). He reviewed search terms and methods that identified the existing systematic reviews, guidelines and meta-analyses, noting that methods did not include review of primary research. The review consisted of published literature rather than beginning from a clinical perspective. Therefore, the input of the stakeholders was and will be key to identify what the literature does not include and to make recommendations of what topics are needed for future systematic reviews.

Melissa McPheeters gave an overview of PICOTS (population, intervention, comparator, outcome, timing and setting) as a tool for helping to describe research questions and decision dilemmas. She stressed that what is *not* available in systematic reviews is more important than what *is* there, and enables the identification of research gaps of great importance.

Stakeholders asked questions regarding heterogeneity of the CP population and whether it is an issue that the research has not yet been done, or if the specific population has not been studied; clarification on the difference between meta-analyses and systematic reviews; clarification on search terms selected; and clarification on which definition of CP was used.

IV. Preliminary Prioritization of Topics to Date

Pam Curtis reviewed the results of the poll to prioritize topics generated prior to the meeting. Items receiving initial high prioritization included lack of standards of care, lack of coordination of care, lack of longitudinal studies, the need for evidence-based care management frameworks, and the comparative effectiveness of treatments for spasticity. She also described the rationale for assignment of participants to small groups to ensure that the greatest possible number of concepts was discussed and a diversity of perspective was represented in each group. Participants were assured that there would be an opportunity to discuss all issues following the small group sessions. Instructions to the small groups were to clarify initial topics (using PICOTS framework), generate potential additional topics, and recommend further prioritization.

V. Small Group Discussions

The participants divided into four small groups for further discussion on the themes of **health care delivery, methods, quality of life, and interventions**.

Health care delivery work group. The health care delivery work group discussed issues related to standards of care as well as translation and application of evidence. The overarching discussion points included:

- Encouragement to use the term “best practices” rather than “standards.”
- An overall lack of data and lack of quality data exists for CP issues, resulting in a lack of guidelines for treatment. The Methods Work Group should consider these issues and highlight the need to use observational data or practice-driven data, the need to include small studies in systematic reviews, the importance of using mixed populations, and the need for long-term studies.
- Outcomes needed include those focused on integration into society, corollary or proxy outcomes, and anticipation of future outcomes that would be important when measuring self-care or exercise for example,
- Current care in CP is piecemeal.
- The Issues Exploration Forum would have been more appropriate if it had built on the work done by existing organizations, agencies, and researchers. The current process is a step backward since those experts apparently were not consulted before beginning the forum.
- Delivery of care is as important a focus area as clinical treatment, requiring inclusion of caregivers and families to help deal with complicated care, most of which is not delivered by clinical providers or in a clinical setting.
- Health care delivery and quality of life are linked.
- All topics should have a life-span and wellness approach.

Priority topics (in no particular order):

- Develop a framework for decisions related to CP, with a care map nested within the framework, including International Classification Framework (ICF) /ICF for children and youth.
- Generate, identify, evaluate and integrate best practices through networks of centers to prospectively enroll children and monitor outcomes related to basic health, self-care, and specialty care.
- Address the lack of coordination of care across the age span and embrace a care model that goes beyond the biomedical model. Include the field of child development and families.
- Address the lack of care coordination practice including translation of information to families, consumers, and clinicians.

Methods workgroup discussion. The methods work group discussed issues related to longitudinal studies, observational research, frameworks, definitions, outcomes, and available methodologies for CP. Major discussion points included:

- The importance of using common definitions of CP that already exist and are recognized internationally.
- Outcomes for research need to be applicable to the patient and family.
- CP is more than a biomedical condition and requires a lifespan research approach, in spite of challenges this approach will present to classical methodological and research designs.
- The need to relay and distribute the Issues Exploration Forum findings to associated bodies—NIH, AHRQ committees, CER methodology groups at HHS.
- Agreement that ongoing stakeholder input in research should be a core value of future methods work.
- The need for evidence generation work, as well as evidence synthesis efforts.

The Methods small group confirmed and refined the following four topics as priorities for future methods work. Priority topics (in no particular order):

- Common nomenclature definitions of CP that already exist like the 2007 international definition of cerebral palsy, and use the World Health Organization International Classification of Functioning, Disability, and Health (ICF) Framework that allows "rule-in" (rather than "rule-out").
- Long-term longitudinal research (both for evidence synthesis and evidence generation) and need more research that addresses subgroup analysis.
- Establish population-wide surveillance program, such as those in Sweden and Australia.
- Long-term stakeholder input should be incorporated in methods and be a core value or principle of all methods work.

Interventions work group. The interventions workgroup discussed issues including surgical, feeding, communication, and durable medical equipment, lack of standardization of care, challenges of existing methodology, lack of primary evidence for synthesis, the need for standardized outcomes measurements and the need for guidelines and best practices for all interventions. The major discussion points included:

- Two overarching comments to be considered:

1. There is no standardization of what outcomes should be measured and how to measure them.
2. There is significant variation in treatment across geographical and patient populations; clinical guidelines are needed for all CP interventions.

- The importance, limitations, and potential long-term benefits vs. harms of surgical interventions. No consensus or guidance on optimal timing and clinical indicators for surgical interventions exists. In addition, there is no comparative evidence regarding surgical interventions versus non-surgical interventions.
- Lack of evidence for post-operative management strategies.
- Long-term functional outcomes are of greatest importance but they are seldom studied.
- There is no consensus or guidance on outcomes measures so each study measures something different. Outcomes measures need to be standardized before evidence synthesis is possible.
- Functional outcomes of importance to people with CP/family members are of the greatest importance to measure. Furthermore, the focus of outcomes measures needs to be on *all* people with CP not just subsets of ambulatory or not, or those with or without communication problems.
- There needs to be assessment of new technologies and treatments, such as deep brain stimulation.
- Speech, language, and communication interventions are not actively and consistently administered. There is a need for systematic guidance for care plans for children with augmented communication.
- Devices are not accessible to many.
- Reimbursement is often not available due to lack of effectiveness of intervention data.
- Clinicians are often not aware of assistive devices that are available indicating a need for better translation and dissemination of what is known to be effective.
- Research needed to determine the effectiveness of devices not designed specifically for disabilities, that is, Ipad for communication. Payers will require this research before paying for devices that are multi-purpose and may be used not only for disability purposes.
- Feeding and nutrition interventions are of great importance as they impact growth and development and all other health outcomes.

Top general research priorities should be in the areas of (in no particular order):

- Identifying interventions that optimize mobility for all with CP whether seated or upright.
- Identifying and addressing issues of chronic pain including interventions that have long-term impact on preventing chronic pain.
- Feeding and nutrition interventions.
- Identifying effective interventions that optimize communication.
- Identifying which interventions facilitate the greatest degree of independent living skills.
- Desire to have tangible outcomes and specific recommendations from this meeting that can be tackled soon.

Priority topics (in no particular order):

- Comparative effectiveness of surgical interventions in particular for hips and their long-term outcomes on mobility and living pain-free.

- Comparative effectiveness of feeding/nutrition interventions.
- Comparative effectiveness of speech and language interventions.
- Assessment of long-term effects of treatments across the lifespan.
- Assessment of benefits and harms of new treatments and technologies.
- Assessment of effectiveness of interventions of independent living or self-care such as feeding, bathing, dressing.
- Sentinel sites need to be used and developed for CP research.
- Common outcomes measures should be implemented.
- Translation, dissemination and implementation especially to clinicians who care for people with CP is needed.

Quality of Life Workgroup Discussion. The quality of life workgroup discussed transition, life span approaches to care, long-term effects of earlier treatments. The quality of life workgroup offered these two overarching comments to be considered by AHRQ:

1. CER is perhaps not the right focus or need since there is a paucity of data.
2. Stakeholder involvement in research discussions is critical. In this area in particular, needs should not be driven by researchers or clinicians alone.

Priority topics (in no particular order):

- The need for more research on aging with CP as the condition changes as a person ages. Research should include lifespan issues, such as sexuality, pregnancy, etc. This should also include issues related to transition of children into the adults system.
- Conduct systematic research on successful models for patient/parent/family and provider engagement with shared decision making. Study the impact of CP on development and the impact on patients and families, instead of studying CP in the context of biomedical and medical disease framework.
- The need for research that helps a patient and family know what they can do to help a child achieve a) maximum physical function b) avoidance of pain as they age through life, and c) developing to the child's maximum potential.
- There is a need for CER to look at the outcomes and need for quality of life measures for CP.
- What is the impact of increased prevention services for children with CP?
- Systematic research is needed on successful models for early and continuous screening for secondary and related conditions.
- Systematic research is needed on successful models for accessible community services.
- Effectiveness of quality of life tools for severe conditions (e.g. quadriplegic, persons on ventilators, and treatment decisions and decision making)
- What evidence is available to support the highest level of education (or other) services, given the reality of resource/budget constraints? What additional information is needed to justify for insurer and/or school systems to pay for services?

VI. Reports from Small Groups

A participant from each small group reported on key discussion points and recommended topics.

Health care delivery group. The group recommended using the term "best practice" instead of "standards of care". They noted the lack of evidence, and that much of the research is on single interventions. There is very little research that looks at overall care coordination across areas or specialties which is the reality for CP. All areas of research should look at outcomes across the lifespan and include a broad perspective. Observational or practice-based studies are needed. Academic centers could do the research to determine the optimal patients, timing, and reasons for specific interventions. Since there is a paucity of health care providers for adults with CP, research on adults could be incorporated into research at specialized pediatric centers. The outcomes of greatest importance are intermediate and long-term outcomes. Important associated issues are general health and well-being. A care path was recommended for patients and families to assist in predicting the course of disease and to help frame choices about treatment and quality of life. Such a care map could include summaries of best practices and best evidence.

Methods group. The methods group discussed the importance of using a standard definition of CP and a common method of classification. ICF is suggested because it encourages the concept of "rule in" versus "rule out" and helps to identify complexity. Outcomes of interest must center on family and patients. Life course issues for people with CP are of great importance. Systematic reviews are currently limited but can help identify gaps in literature that lead to opportunities for knowledge generation. As noted by other groups, there is significant opportunity to opportunity to develop and evaluate methods for CP, especially for longitudinal studies, and to use multivariate analysis for CP. Current methods are not conducive to long-term follow-up studies. Surveillance and registries can assist and allow for needed subgroup analyses, for tracking relevant data, and for allowing for larger numbers of participants. AHRQ should engage in more active dissemination to let people know about the availability of the reports that already exist. Patients and families must be seen as partners in research.

Interventions group. This group believed it important to prioritize interventions that occur across populations and have a dynamic effect over time (e.g., how do childhood surgeries impact long-term outcomes of pain and mobility?). The group discussed the interrelatedness of interventions and the lack of evidence or research methods to study the complexity of a condition like CP. Interventions are delivered as a package of care and should be studied in their complexity. For example, surgery may be offered along with other interventions such as Botox injections. Existing evidence is outdated and does not allow for combinations of interventions and long term impacts.

Feeding and nutrition interventions are of great importance and should be given top priority. Studies need to be expanded beyond just children to include adult populations. Outcomes should focus on function and include social inclusion, optimal participation, and functioning especially as related to independent living. Effectiveness research should be based on prospective cohort studies conducted at "sentinel sites" or centers that treat the spectrum of CP conditions holistically and look at long-term functional outcomes by collecting data across locations and time. Systematic barriers to access and disparities, especially in treatments and devices including communication technologies, should be identified and addressed. Translation, dissemination and implementation of evidence-based information should be available to all impacted populations including patients, families, clinicians, and payers.

Quality of life group. The Quality of Life (QOL) group discussed the importance of including family members and patients in all decisions of both treatment and research, especially when identifying outcomes of importance. There is a lack of clear and consistent measurement of quality of life, yet this measure should be included in the equation for all decision-making. QOL should be defined by patients and families rather than by researchers or clinicians. Pain, in particular, is often overlooked for patients with CP. Capacity measures of family strengths are needed. There should be a comparative effectiveness review of community supports versus other interventions (Botox, surgery, etc.). In-home support services may increase QOL, but cost effectiveness of services has not been studied. QOL must be measured pre- and post-intervention in order to be meaningful.

The group discussed issues related to aging with CP and transitions from child system services to adult services. Social preparation, educational preparation, and psychological preparation all need to be considered in transition phases. Provision of services should be modified according to cultural differences. There should be a registry of adults and children with CP that could help address some of the issues of QOL and transitions. In addition, evidence-based decision and guidance tools should be developed.

VII. Final Prioritization

Pam Curtis noted that there were several themes that emerged from the small groups. These included (in no particular order):

- The need to take a "life course" approach to all CP work that "rules in" rather than "rules out" conditions and needs.
- The need to take an integrated approach that considers emotional, psycho-social, and other aspects of consumer lives.
- An inclusive view of care delivery, given that the majority of care is not provided in clinical settings.
- The importance of consumer and family involvement.
- The importance of considering cultural variables and cultural appropriateness.
- The need for longitudinal study of CP and the impact of CP treatment over time.
- The importance of adopting standard outcomes and measures.

In addition, the specific activities or studies prioritized by small groups seemed to readily group into four research activities:

1. **Evidence Synthesis**: Topics that may be ready for CER. These include issues of mobility, (wheelchairs, use of standers), feeding/eating/nutrition, communication/speech, care coordination, social supports vs. medical vs. pharmacologic treatments in quality of life, impact of services on quality of life, subgroup analysis of existing meta-analyses (for example existing orthotics report), surgical vs. pharmacological interventions with specification of clinical or cost effectiveness (quality adjusted life years), and the need for technology assessments.
2. **Methods and Evidence Generation**: This category includes the call for networks of centers that could conduct research including clinical practice research, longitudinal studies, sub-group analyses, and multivariate analyses. There was also a call for registries, standardization of outcomes measures, and involvement of consumers and families as partners in research,

3. **Translation and Dissemination**: This category includes the need for translational products for different audiences (clinicians, patients and families, educators, payers), summaries of the evidence that are regularly updated, use of family friendly websites or social marketing, plain language reports or fact sheets, presentations to parent/patient/advocacy groups, active outreach and dissemination efforts to organizations interested in CP, and a concentrated effort to reach clinicians who treat adults with CP.
4. **Development of a Framework and other research activities**: This category includes the need for a framework and care pathway, common definitions, consensus on best practices, convening panels on issues such as pain, and meetings of payers to discuss evidence and commonly denied services.

VIII. Wrap Up and Next Steps

Pam Curtis and Shilpa Amin thanked the group for their participation. Shilpa Amin reviewed the next steps. Based on conversations over the course of the forum there may be a greater need for evidence reviews, technical briefs, and work by the DEcIDES network and other AHRQ portfolio program mechanisms. AHRQ may initially need to focus here rather than on comparative effectiveness reviews. There were many topics generated by forum participants that can now be refined for nomination to the EHC Program. Vanderbilt will produce a white paper that will summarize the forum processes. AHRQ is looking for opportunities to work with other Federal partners to advance the research agendas of stakeholders. Shilpa encouraged participants to visit the website and sign up for the AHRQ EHC Program notifications and to inform AHRQ of stakeholder and end-user interests to further participate in AHRQ initiatives and research.

IX. Adjourn

The meeting was adjourned at 3:00 pm.

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