

Evidence-based Practice Center Comparative Effectiveness Review Protocol

Project Title: Feeding and Nutrition Interventions in Cerebral Palsy

I. Background and Objectives for the Systematic Review

Cerebral palsy (CP) is “a group of permanent disorders of the development of movement and posture, causing activity limitations, 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 secondary musculoskeletal problems.”¹ This group of syndromes range in severity and are the result of a variety of etiologies occurring in the prenatal, perinatal, or postnatal period. Though the disorder is nonprogressive, the clinical manifestations may change over time as the brain develops, with other neurologic impairments frequently co-occurring.

CP is the most common cause of motor disability in children. Prevalence estimates in the United States over the past 20 years have been approximately 2 to 4 cases per 1,000 children under the age of 18, with spastic CP being the most common subtype.²⁻¹⁰ More than 100,000 children are estimated to be affected in the United States. Due to advances in supportive medical care, approximately 90 percent of children with CP survive into adulthood, resulting in an additional estimated 400,000 adults living with CP in the United States.¹¹⁻¹⁶ Lifetime costs are estimated to be nearly \$1,000,000 per person.¹⁷

Classification and Spectrum of Disorder

CP includes a spectrum of disorders of movement, posture, and coordination with heterogeneous etiologies. The diversity of the clinical features is reflected in multiple classification systems that include reference to type of motor dysfunction, body parts affected, severity, and functional abilities (see Table 1).

Of note, in classifying on motor function, spastic CP accounts for 70 to 80 percent of all cases of CP, with dyskinetic accounting for 10 to 15 percent and ataxic for 15 percent, though combinations of clinical manifestations are common. Further classification is by severity level (mild, moderate, severe) and gross motor function (GMFCS), which reflects the functional capabilities of the affected.^{18,19} The GMFCS includes levels that reflect abilities ranging from walking without limitations (level 1) to severe head and trunk control limitations that require extensive use of assisted technology, physical assistance, and a wheelchair (level 5).

Although CP is a motor disorder, many children and adults with CP suffer with other developmental disabilities, including intellectual disability, impaired vision and hearing, language and behavioral disorders, and epilepsy. Population-based studies have reported the proportion of children with CP who have intellectual disability ranges from 31 to 65 percent, and the proportion that have epilepsy ranges from 20 to 46 percent.¹⁹⁻²¹ Intellectual disability varies with subtype of CP and level of impairment.^{11, 21-23} Survival and quality of life vary across the spectrum of CP but are associated with severity, functional disabilities, and comorbid conditions.²⁴

Table 1. CP classification systems used and understood by qualified medical practitioners (www.cerebralpalsy.org)

Severity Level	Topographical Distribution	Motor Function	Gross Motor Function Classification System
<ul style="list-style-type: none"> • Mild: child can move without assistance; his or her daily activities are not limited. • Moderate: child will need braces, medications, and adaptive technology to accomplish daily activities. • Severe: child will require a wheelchair and will have significant challenges in accomplishing daily activities. • No CP: child has cerebral palsy signs, but the disorder was acquired after completion of brain development and is therefore classified under the incident that caused the cerebral palsy, such as traumatic brain injury or encephalopathy. 	<ul style="list-style-type: none"> • Monoplegia/monoparesis means only one limb is affected. It is believed this may be a form of hemiplegia/hemiparesis where one limb is significantly impaired. • Diplegia/diparesis usually indicates the legs are affected more than the arms; primarily affects the lower body. • Hemiplegia/hemiparesis indicates the arm and leg on one side of the body is affected. • Paraplegia/paraparesis means the lower half of the body, including both legs, are affected. • Triplesia/triparesis indicates three limbs are affected. This could be both arms and a leg, or both legs and an arm. Or, it could refer to one upper and one lower extremity and the face. • Double hemiplegia/double hemiparesis indicates all four limbs are involved, but one side of the body is more affected than the other. • Tetraplegia/tetraparesis indicates that all four limbs are involved, but three limbs are more affected than the fourth. • Quadriplegia/quadriparesis means that all four limbs are involved. • Pentaplegia/pentaparesis means all four limbs are involved, with neck and head paralysis often accompanied by eating and breathing complications. 	<ul style="list-style-type: none"> • Spastic: implies increased muscle tone. Muscles continually contract, making limbs stiff, rigid, and resistant to flexing or relaxing. Reflexes can be exaggerated, while movements tend to be jerky and awkward. Often, the arms and legs are affected. The tongue, mouth, and pharynx can be affected, as well, impairing speech, eating, breathing, and swallowing. Spastic cerebral palsy is hypertonic and accounts for 70% to 80% of cerebral palsy cases. The injury to the brain occurs in the pyramidal tract and is referred to as upper motor neuron damage. • Non-Spastic: decreased and/or fluctuating muscle tone. Multiple forms of non-spastic cerebral palsy are each characterized by particular impairments; one of the main characteristics of non-spastic cerebral palsy is involuntary movement. Movement can be slow or fast, often repetitive, and sometimes rhythmic. Planned movements can exaggerate the effect – a condition known as intention tremors. Stress can also worsen the involuntary movements, whereas sleeping often eliminates them. An injury in the brain outside the pyramidal tract causes non-spastic cerebral palsy. Due to the location of the injury, mental impairment and seizures are less likely. Non-spastic cerebral palsy is divided into two groups, ataxic and dyskinetic. Together they make up 20% of cerebral palsy cases. Broken down, dyskinetic makes up 15% of all cerebral palsy cases, and ataxic comprises 5%. 	<p>The GMFCS uses head control, movement transition, walking, and gross motor skills such as running, jumping, and navigating inclined or uneven surfaces to define a child's accomplishment level. The goal is to present an idea of how self-sufficient a child can be at home, at school, and at outdoor and indoor venues.</p> <ul style="list-style-type: none"> • GMFCS Level I: walks without limitations. • GMFCS Level II: walks with limitations. Limitations include walking long distances and balancing, but not as able as Level I to run or jump; may require use of mobility devices when first learning to walk, usually prior to age 4; and may rely on wheeled mobility equipment when outside of home for traveling long distances. • GMFCS Level III: walks with adaptive equipment assistance. Requires hand-held mobility assistance to walk indoors, while utilizing wheeled mobility outdoors, in the community and at school; can sit on own or with limited external support; and has some independence in standing transfers. • GMFCS Level IV: self-mobility with use of powered mobility assistance. Usually supported when sitting; self-mobility is limited; and likely to be transported in manual wheelchair or powered mobility. • GMFCS Level V: severe head and trunk control limitations. Requires extensive use of assisted technology and physical assistance; and transported in a manual wheelchair, unless self-mobility can be achieved by learning to operate a powered wheelchair.
<p>Cerebral palsy is often classified by severity level as mild, moderate, severe, or no CP. These are broad generalizations that lack a specific set of criteria. Even when doctors agree on the level of severity, the classification provides little specific information, especially when compared to the GMFCS. Still, this method is common and offers a simple method of communicating the scope of impairment, which can be useful when accuracy is not necessary.</p>	<p>When used with motor function classification, this provides a description of how and where a child is affected by cerebral palsy.</p>		

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Feeding Difficulties and Interventions

Individuals with CP frequently have feeding and swallowing problems that may lead to poor nutritional status, growth failure, chronic aspiration, esophagitis, and respiratory infections. Across the CP spectrum, poor nutritional status is caused by distinct pathways ranging from inadequate intake, oral dysphagia, oropharyngeal dysphagia, gastroesophageal reflux (GER), and chronic aspiration. Some patients with oropharyngeal dysphagia and GER, particularly those with severe CP, are also at risk for recurrent aspiration that can lead to chronic pulmonary disease. Patients with feeding difficulties range from those with self-feeding skills to those with severe disability (GMFCS V) who require extensive use of assisted technology and are dependent on others to feed them. Indeed, chronic pulmonary disease related to aspiration is the leading cause of death among patients with severe CP. Data suggest that during the first year of life, 57 percent of children with CP have sucking problems, 38 percent have swallowing problems, 80 percent have been fed nonorally on at least one occasion, and more than 90 percent have clinically significant oral motor dysfunction.²⁵ More severe motor impairment is associated with greater difficulty with swallowing.²⁶ Among children with spastic quadriplegia, one third have been reported to require assisted feeding.²⁷ Individuals with severe functional limitations (GMFCS level IV or V) commonly need assisted feeding. Caregiver burden is also a significant concern, as the feeding process may require considerable time and may be associated with stress and caregiver fatigue.²⁸

A number of feeding and oral-motor intervention strategies have been developed to address difficulties with sucking, chewing, swallowing and to improve oral-motor skills, including oral sensorimotor management, positioning, oral appliances, food thickeners, specialized formulas, and neuromuscular stimulation. These interventions address different aspects of feeding difficulties, reflecting the range in specific problems associated with feeding and nutrition in patients with CP. Sensorimotor techniques seek to strengthen oral-motor control and counteract abnormal tone and reflexes to improve oral feedings and typically require months of daily application. Positioning techniques address poor postural alignment and control that exacerbates swallowing difficulties and include stabilizing the neck and trunk. Positioning interventions are individualized and often guided by videofluoroscopy to optimize swallowing. Oral appliances have been used to stabilize the jaw and improve sucking, tongue coordination, lip control, and chewing. Multiple approaches may be used in children with growth failure, including sensorimotor stimulation, positioning, food thickeners, and caloric supplementation. For children with moderate to severe aspiration or malnutrition related to oropharyngeal dysphagia and GER, surgical interventions with gastrostomy (tube feeding directly into the stomach) or jejunostomy tubes and antireflux procedures may be necessary to improve nutritional status and reduce risk of chronic aspiration.^{28,29}

Clinical Uncertainties

The goal for management of CP is to improve the quality of life for both the child and family, through interventions that maximize independence in activities of daily living, mobility, and nutrition. Guidelines have been published by the American Academy of Neurology on the use of pharmacologic agents to treat spasticity in children and adolescents with CP.³⁰ However, there is a limited evidence base for the majority of CP interventions, including those that address nutrition and growth.³¹ Despite a range of potential feeding interventions for patients with CP, synthesis is lacking on the efficacy, safety, and applicability of these interventions. Limited information is available on the impact on long-term health outcomes, including quality of life.

Despite the availability of multiple and diverse interventions to address feeding difficulties, the optimal combination of interventions and the effectiveness in different patient populations with CP is unknown. Consideration of effectiveness likely depends on the type of CP (spastic or nonspastic), the location of motor involvement (e.g., diplegia, quadriplegia), and functional status, including ability to walk or sit and the degree of head and trunk control. Comorbid conditions, particularly intellectual disability (related to ability to monitor and maintain appropriate nutrient intake), and concurrent medications that potentially have gastrointestinal side effects may influence treatment outcomes. Different feeding interventions may perform differently across the spectrum of CP. For example, oral-motor interventions may be highly effective in populations with oral dysphagia with malnutrition. However, these same interventions could have less value in less mobile populations who are experiencing pharyngeal dysphagia with aspiration. Gastrostomy feeding may reduce aspiration during swallowing but does not address aspiration of oral secretions and could exacerbate GER. Additional interventions, such as positioning and caloric supplementation, may still be needed. To examine the overall effectiveness of interventions intended to improve feeding and nutrition outcomes in patients with CP, adequate characterization of the patient populations will be essential. Additionally, the need for management into later life has increased, and the optimal interventions for adults with feeding difficulties are unknown.^{16, 32}

Harms associated with feeding interventions have not been thoroughly reviewed, and significant concerns have been raised about potential serious harms related to surgical interventions, including new or worsening GER, risk of aspiration, and mortality. The impact of antireflux procedures in addition to gastrostomy is also unknown. Finally, there is a need to understand the potential impact of feeding interventions on families and caregivers as substantial caregiver time and training may be required.

CP is a significant health problem with major effects over the lifespan. Feeding difficulties related to CP can affect an individual's nutritional and growth status and quality of life, as well as contribute to comorbidities including respiratory conditions and gastrointestinal symptoms. Feeding difficulties affect individuals with CP of all ages and severity levels. Considerable uncertainty remains regarding the appropriate interventions, especially in older individuals.

II. The Key Questions

We developed our Key Questions (KQs) and Population-Intervention-Comparators-Outcomes-Timing-Setting (PICOTS) parameters in consultation with our key informants/Technical Expert Panel (TEP) members and Task Order Officer (TOO).

Our KQs were posted for public comment on the Effective Health Care Program Web site from April 18 to May 16, 2012. We received few actionable comments, and none required revisions to the KQs: One comment addressed the need to consider the effect of tube feeding on pulmonary toilet, including effects on chest percussion therapy and other modalities, in assessing effectiveness. Another comment noted the importance of considering the quality of nutritional substances in addition to the quantity.

Our final KQs are as follows:

KQ1a. When compared with other nonsurgical interventions or no intervention, how effective are behavioral interventions, including positioning, oral appliances, oral stimulation, sensorimotor facilitation, and caregiver training, for improving nutritional state/growth,

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health outcomes, health care/resource utilization, and quality of life in individuals with CP and feeding difficulties?

- KQ1b.** Is the effectiveness of behavioral interventions modified by age, race, severity, functional status (e.g., GMFCS level), or initial nutritional status?
- KQ2a.** When compared with other nonsurgical interventions or no intervention, how effective are nutritional interventions (food thickeners, caloric supplementation with formulas, vitamin supplementation, and altering food consistency [e.g., pureeing]) for improving nutritional state/growth, health outcomes, health care/resource utilization, and quality of life in individuals with CP and feeding difficulties?
- KQ2b.** Is the effectiveness of nutritional interventions modified by age, race, severity, functional status (e.g., GMFCS level), or initial nutritional status?
- KQ3a.** What is the comparative effectiveness of tube feeding when compared with oral feeding or with nutritional and behavioral interventions in individuals with CP who present with feeding difficulties, including malnourishment, failure to thrive, aspiration, and excessive caregiver burden?
- KQ3b.** Among individuals with CP and feeding difficulties *with significant reflux*, what is the effectiveness of g-tube placement with fundoplication versus oral feeding for reducing reflux and for improving nutritional state/growth, health outcomes, health care/resource utilization, and quality of life?
- KQ3c.** Among individuals who develop reflux after gastrostomy, what is the comparative effectiveness of j-tube versus fundoplication for reducing reflux in the short term and achieving improvements in nutritional state/growth, health outcomes, health care/resource utilization, and quality of life?
- KQ3d.** Is the effectiveness of tube feeding modified by tube placement, age, race, severity, functional status (e.g., GMFCS level), initial nutritional status, or continuous versus bolus feeding?

For each KQ, the relevant population, interventions, comparators, outcomes, timing, and setting are as follows:

PICOTS for Key Question 1

Population

Individuals with CP and feeding difficulties (all ages and severities)

Interventions

Positioning, oral appliances, oral stimulation, sensorimotor facilitation, and caregiver training

Comparators

Other nonsurgical interventions

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Outcomes

- Intermediate or surrogate outcomes:
 - Growth status as proxies for nutrition (height including leg length or tibia length, weight, skinfold status, and energy expenditure)
 - Nutritional status (measures of energy balance and micronutrient scores)
 - Improved swallowing (including feeding efficiency score)
 - Need for surgical or nutritional intervention

- Patient-centered and health outcomes:
 - Mortality
 - Hospitalizations
 - Days of antibiotics for aspiration needed
 - Validated measures of quality of life (e.g., SF-36, CAPE, HRQOL)
 - Patient and family satisfaction and stress
 - Decreased parent/caregiver time spent on feeding-related activities
 - Physical and mental health of primary caregiver
 - Other gastrointestinal symptoms
 - Reflux outcomes (episodes of reflux and duration)

- Adverse effects including but not limited to:
 - Episodes of aspiration, pneumonia or acute respiratory problems, asthma, or other respiratory markers
 - Pain/comfort
 - Diarrhea
 - Other gastrointestinal symptoms (e.g., constipation, retching, dumping, gas-bloat syndrome, secondary GER)
 - Obstruction

Time

No limit

Settings

All settings will be considered (e.g., home, clinic, hospital, institutional settings)

PICOTS for Key Question 2

Population

Individuals with CP and feeding difficulties (all ages and severities)

Interventions

Food thickeners, caloric supplementation with formulas, vitamin supplementation, and altering food consistency (e.g., pureeing)

Comparators

Other nonsurgical interventions

Outcomes

- Intermediate or surrogate outcomes:
 - Growth status as proxies for nutrition (height including leg length or tibia length, weight, skinfold status, and energy expenditure)
 - Nutritional status (measures of energy balance and micronutrient scores)
 - Mortality
 - Improved swallowing (including feeding efficiency score)
 - Need for surgical or nutritional intervention
- Patient-centered and health outcomes:
 - Hospitalizations
 - Days of antibiotics for aspiration needed
 - Validated measures of quality of life (e.g., SF-36, CAPE, HRQOL)
 - Patient and family satisfaction and stress
 - Decreased parent/caregiver time spent on feeding-related activities
 - Physical and mental health of primary caregiver
 - Other gastrointestinal symptoms
 - Reflux outcomes (episodes of reflux and duration)
- Adverse effects including but not limited to:
 - Episodes of aspiration, pneumonia or acute respiratory problems, asthma or other respiratory markers
 - Pain/comfort
 - Diarrhea
 - Other gastrointestinal symptoms (e.g., constipation, retching, dumping, gas-bloat syndrome, secondary GER)
 - Obstruction

Time

No limit

Settings

All settings will be considered (e.g., home, clinic, hospital, and institutional settings)

PICOTS for Key Question 3a

Population

Individuals with CP and feeding difficulties but without reflux (all ages and severities)

Interventions

Tube feeding via g-tube or j-tube with or without fundoplication

Comparators

Nonsurgical feeding interventions (behavioral and nutritional) or oral feeding (no intervention)

Outcomes

- Intermediate or surrogate outcomes:
 - Growth status as proxies for nutrition (height including leg length or tibia length, weight, skinfold status, and energy expenditure)
 - Nutritional status (measures of energy balance and micronutrient scores)
 - Improved swallowing (including feeding efficiency score)
 - Need for surgical or nutritional intervention
- Patient-centered and health outcomes:
 - Mortality
 - Hospitalizations
 - Days of antibiotics for aspiration needed
 - Validated measures of quality of life (e.g., SF-36, CAPE, HRQOL)
 - Patient and family satisfaction and stress
 - Decreased parent/caregiver time spent on feeding-related activities
 - Physical and mental health of primary caregiver
 - Other gastrointestinal symptoms
 - Reflux outcomes (episodes of reflux and duration)
- Adverse effects including but not limited to:
 - Failure to place tube or tube migration/dislodgment
 - Need for further surgery
 - Gastrointestinal bleeding or ulceration
 - Peritonitis
 - Interference with pulmonary toilet
 - Episodes of aspiration, pneumonia or acute respiratory problems, asthma, or other respiratory markers
 - Pain/comfort
 - Other gastrointestinal symptoms (e.g., constipation, retching, dumping, gas-bloat syndrome, secondary GER)

Time

No limit

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Settings

All settings will be considered (e.g., home, clinic, hospital, institutional settings)

PICOTS for Key Question 3b

Population

Individuals with CP and feeding difficulties with significant reflux (all ages and severities)

Interventions

G-tube with fundoplication

Comparators

Oral feeding

Outcomes

- Intermediate or surrogate outcomes:
 - Growth status as proxies for nutrition (height including leg length or tibia length, weight, skinfold status, and energy expenditure)
 - Nutritional status (measures of energy balance and micronutrient scores)
 - Improved swallowing (including feeding efficiency score)
 - Need for surgical or nutritional intervention
- Patient-centered and health outcomes:
 - Mortality
 - Hospitalizations
 - Days of antibiotics for aspiration needed
 - Validated measures of quality of life (e.g., SF-36, CAPE, HRQOL)
 - Patient and family satisfaction and stress
 - Decreased parent/caregiver time spent on feeding-related activities
 - Physical and mental health of primary caregiver
 - Other gastrointestinal symptoms
 - Reflux outcomes (episodes of reflux and duration)
- Adverse effects including but not limited to:
 - Failure to place tube or tube migration/dislodgment
 - Need for further surgery
 - Gastrointestinal bleeding or ulceration
 - Peritonitis
 - Interference with pulmonary toilet

- Episodes of aspiration, pneumonia or acute respiratory problems, asthma, or other respiratory markers
- Pain/comfort
- Other gastrointestinal symptoms (e.g., constipation, retching, dumping, gas-bloat syndrome, secondary GER)

Time

No limit

Settings

All settings will be considered (e.g., home, clinic, hospital, institutional settings)

PICOTS for KQ3c

Population

Individuals with CP and feeding difficulties who initially present without reflux but develop reflux following g-tube placement (all ages and severities)

Interventions

J-tube or fundoplication

Comparators

J-tube or fundoplication; compared with the other intervention

Outcomes

- Intermediate or surrogate outcomes:
 - Growth status as proxies for nutrition (height including leg length or tibia length, weight, skinfold status, and energy expenditure)
 - Nutritional status (measures of energy balance, micronutrient scores)
 - Improved swallowing (including feeding efficiency score)
 - Need for surgical or nutritional intervention
- Patient-centered and health outcomes:
 - Mortality
 - Hospitalizations
 - Days of antibiotics for aspiration needed
 - Validated measures of quality of life (e.g., SF-36, CAPE, HRQOL)
 - Patient and family satisfaction and stress
 - Decreased parent/caregiver time spent on feeding-related activities
 - Physical and mental health of primary caregiver
 - Other gastrointestinal symptoms



- Reflux outcomes (episodes of reflux and duration)
- Adverse effects including but not limited to:
 - Failure to place tube or tube migration/dislodgment
 - Need for further surgery
 - Gastrointestinal bleeding or ulceration
 - Peritonitis
 - Interference with pulmonary toilet
 - Episodes of aspiration, pneumonia or acute respiratory problems, asthma, or other respiratory markers
 - Pain/comfort
 - Other gastrointestinal symptoms (e.g., constipation, retching, dumping, gas-bloat syndrome, secondary GER)

Time

No limit

Settings

All settings will be considered (e.g., home, clinic, hospital, institutional settings)

III. Analytic Framework

The analytic framework in Figure 1 illustrates the population, interventions, and outcomes that will guide the literature search and synthesis. Circles on the diagram indicate areas in which KQs will be addressed in the review.

Figure 1: Analytic framework for Feeding and Nutrition Interventions in Cerebral Palsy

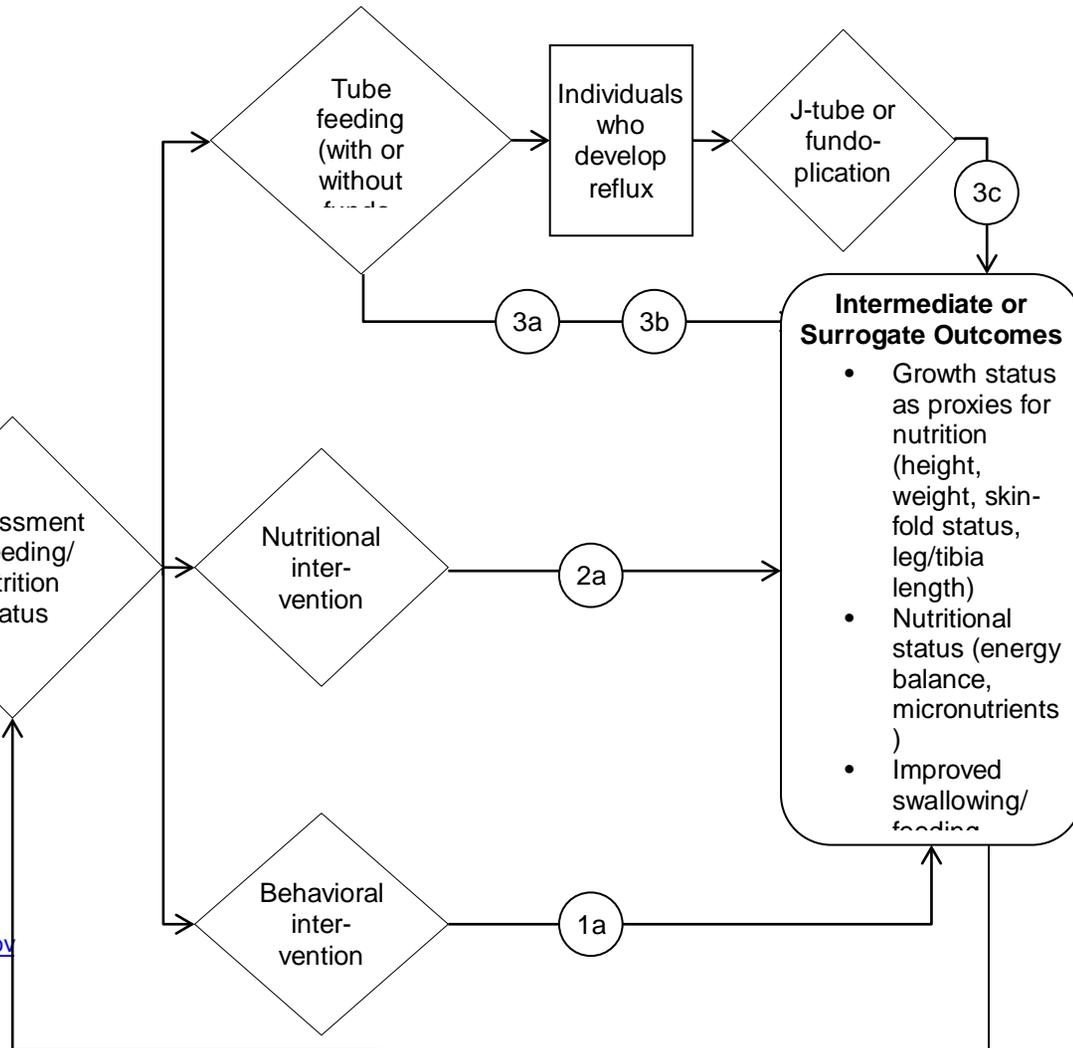


Type of Cerebral Palsy (CP) and Other Characteristics:	
Severity of CP (mild, moderate, severe)	Intellectual and clinical comorbidities
Topographical distribution of CP (monoplegia to pentaplegia)	Severity of intellectual disability
Spastic or non-spastic (dyskinetic and ataxic) CP	Caregiver/family needs
Gross Motor Function Classification System level	Initial nutritional status
Age	Tube placement
Race	Continuous vs bolus feeding

- 1b
- 2b
- 3d

Individuals with CP who present with feeding and nutrition problems indicated by:

- signs of malnourishment/failure to thrive
- episodes of aspiration/pneumonia
- swallowing difficulties
- other clinical concerns for nutritional support



- Patient-Centered and Health Outcomes**
- Mortality
 - Hospitalizations (number and length of stay)
 - Days of antibiotics needed
 - Validated measure of quality of life
 - Patient and family satisfaction and stress
 - Decreased time spent on feeding-related activities
 - Physical and mental health of primary caregiver
 - Pain/comfort
 - Reflux outcomes
 - Other gastrointestinal symptoms
 - Adverse outcomes, including

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Nutritional interventions: food thickeners, caloric supplementation with formulas, vitamin supplementation, altering food consistency
Behavioral interventions: positioning, oral appliances, oral stimulation, sensorimotor facilitation, caregiver training



Abbreviations: CP = cerebral palsy

IV. Methods

A. Criteria for Inclusion/Exclusion of Studies in the Review

We outline the inclusion/exclusion criteria selected based on our understanding of the literature, input from the topic refinement phase and content experts, and established principles of methodological quality in Table 2. We will conduct searches from 1980 to the present to ensure comprehensive retrieval. We will limit retrieval to English-language studies only as we identified a high number of international studies in our initial scan of the literature and feel that globally relevant studies are likely being identified. Further, in the opinion of our TEP, most studies of relevance in the area are published in English.

Table 2. Inclusion/exclusion criteria

Category	Criteria
Study population	<ul style="list-style-type: none"> Individuals with CP and feeding or nutrition difficulties
Time period	<ul style="list-style-type: none"> 1980–present
Publication languages	<ul style="list-style-type: none"> English only
Admissible evidence (study design and other criteria)	<p><u>Admissible designs</u></p> <ul style="list-style-type: none"> Controlled trials, observational studies including prospective and retrospective cohort studies, prospective and retrospective case series providing data from before and after intervention, and systematic reviews <p><u>Other criteria</u></p> <ul style="list-style-type: none"> Original research studies that provide sufficient detail regarding methods and results to enable use and adjustment of the data and results Patient populations must include individuals with CP (at least 80% for studies with mixed populations not reporting data separately for individuals with CP) and feeding or nutrition difficulties Studies must address one or more of the following: <ul style="list-style-type: none"> Nonsurgical interventions Behavioral interventions (including positioning, oral appliances, oral stimulation, sensorimotor facilitation, and caregiver training) Nutritional interventions Tube feeding Oral feeding Surgical interventions (G-tube, J-tube, fundoplication) Modifiers of nonsurgical intervention effectiveness (age, race, severity, functional status) Modifiers of tube feeding effectiveness (tube placement, age, race, severity, functional status, initial nutritional status, or continuous vs. bolus feeding) Baseline and outcome data (including harms) related to interventions for feeding difficulties Studies must include extractable data on relevant outcomes, including data presented in text or tables (vs. solely in figures) Studies must provide aggregate data vs. data for each individual participant

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Abbreviations: CP = cerebral palsy

B. Searching for the Evidence: Literature Search Strategies for Identification of Relevant Studies To Answer the Key Questions

- 1. Databases.** To ensure comprehensive retrieval of relevant studies addressing CP and feeding difficulties, we will use six key databases including studies related to surgical and nonsurgical interventions for promoting feeding and nutrition in individuals with CP: the MEDLINE[®] medical literature database via the PubMed[®] interface, the PsycINFO[®] psychology and psychiatry database, the Cumulative Index of Nursing and Allied Health Literature (CINAHL[®]), the OTSeeker database, REHABDATA, and the Education Resources Information Center database (ERIC[®]). The search strategies for each of these databases will focus specifically on terms related to CP and nutrition/feeding-focused interventions, including keywords, subject headings, and a combination of subject headings and/or keywords (e.g., CP, cerebral palsy, enteral feeding, occupational therapy, etc.). All searches will be created by an expert librarian and reviewed by a second expert librarian. See Appendix A for search strategies.
- 2. Search updates.** We will update the search when the draft report is submitted and add relevant studies as needed while the draft report is undergoing peer review. We will also incorporate studies that meet our inclusion criteria or are relevant as background material that may be identified by both public and peer reviewers or via Scientific Information Packets (see below).
- 3. Hand searching.** We will carry out hand searches of the reference lists of recent systematic reviews or meta-analyses of feeding interventions for individuals with CP; the investigative team will also scan the reference lists of articles that are included after the full-text review phase for studies that potentially could meet our inclusion criteria.
- 4. Grey literature.** We will request Scientific Information Packets and regulatory information searches addressing those devices with FDA-approval for ameliorating feeding difficulties associated with CP (VitalStim[®]). We will review abstracts from the past 2 years presented at the annual meetings of key scientific societies (American Academy for Cerebral Palsy and Developmental Medicine and the American Academy of Physical Medicine and Rehabilitation).
- 5. Review of reviews.** We will use Evidence-based Practice Center methods as outlined by White et al. in the *Methods Guide for Comparative Effectiveness Reviews*³³ to conduct a review of systematic reviews addressing feeding and nutrition interventions for CP. We will use our MEDLINE search strategy to identify systematic reviews published from 1980 to the present. We will assess the quality of systematic reviews using the AMSTAR measurement tool (Appendix B).

We will summarize results of those reviews assessed as higher quality in the current CER and augment the summary with results of studies meeting our inclusion criteria and not addressed in prior reviews. We anticipate adapting or including (with appropriate permissions) relevant results tables from prior reviews to ensure that evidence assessed in prior reviews meeting our criteria is presented in sufficient detail to inform

decisionmaking. Based on our initial scan of the literature, we anticipate that a recent review addressing behavioral interventions²⁸ and one addressing gastrostomy³⁸ may be good candidates for this approach.

C. Data Abstraction and Data Management

- 1. Data-extraction forms:** We will develop data-collection forms for the abstract review, the full-text review, and data extraction into evidence tables. The forms used for the abstract review will contain questions about the primary exclusion and inclusion criteria. The forms used for the full-text review are more detailed and are intended to assist in a) identifying studies that meet inclusion criteria and b) initially sorting the studies according to the KQs. Finally, data-extraction forms will collect those data necessary to create evidence tables and perform data synthesis. Design of the forms will be informed by guidance³⁴ provided by the Agency for Healthcare Research and Quality Effective Health Care Program, as well as standards put forth by the American Academy for Cerebral Palsy and Developmental Medicine (AACPD), which specify the reporting of data describing the intervention, population, number of subjects, research methods, and outcomes.³⁵

We will also collect data on modifiers of interest as specified in KQs 2b and 3d, specifically age, race, severity, functional status, initial nutritional status, and continuous or bolus feeding. The form also will include a field in which to report the funding source of a study.

After reviewing a sample of relevant articles, the methods lead and project manager will design the data-collection forms and test them on multiple articles before beginning each stage of data extraction. We expect that the data-collection forms will undergo several revisions as these tests are completed.

- 2. Initial review of abstracts.** We will review all the titles and abstracts identified through our searches against our inclusion/exclusion criteria. Each abstract will be reviewed by at least two members of the investigative team. When differences between the reviewers arise, we will err on the side of inclusion. For studies without adequate information to make the determination, we will retrieve the full-text articles and review them against the inclusion/exclusion criteria.
- 3. Retrieving and reviewing articles.** We will retrieve and review all articles that meet our predetermined inclusion criteria or for which there is insufficient information in the abstract to make a decision about eligibility. Each article will be reviewed by at least two members of the investigative team. Differences between the reviewers will be adjudicated by a third party.
- 4. Deciding which outcomes are to be extracted.** We identified areas in which to extract outcomes based on our clinical expertise and our initial scan of the literature. Our final list of outcomes includes the following: growth status as proxies for nutrition (height [including leg length/tibial length], weight, skinfold status, and energy expenditure), improved swallowing (including feeding efficiency scores), need for behavioral or nutritional intervention, nutritional status, mortality, hospitalizations, days of antibiotics needed, validated measures of quality of life, patient and family satisfaction and stress, decreased time spent on feeding-related activities, physical and mental health of primary

caregiver, reflux outcomes, other gastrointestinal symptoms, and harms of interventions, including adverse effects of tube feeding on pulmonary toilet, as reported.

For studies that meet the conditions of the second-round assessment, the abstractors will extract key data and study-quality elements from the article(s) and enter them into evidence tables. As noted above, we anticipate that these elements will include population and intervention characteristics such as age, functional status, and intervention approach; study design/methodological characteristics; and outcomes reported. A second reviewer will review those data-extraction forms against the original articles for quality control. Differences in data coding between the abstractor and the reviewer will be resolved by consensus.

We will develop a simple categorization scheme for coding the reasons that articles, at the stage of full review, are not finally included in the report. The abstractor will note the reason(s) for exclusion on the article abstraction form. We will then record those codes in an EndNote® (Thomson Reuters, New York, NY) bibliographic database so that we can later compile a listing of excluded articles and the reasons for such exclusions.

D. Assessment of Methodological Risk of Bias of Individual Studies

We will assess the quality of studies using the following established tools (Appendix B) for various study types:

- For randomized trials, we will use the Cochrane risk of bias tool.
- For case-control and cohort studies, we will use the Newcastle-Ottawa scale.
- For case series, we will use a tool adapted from EPC work to develop methods to assess risk of bias.³⁶
- For systematic reviews, we will use the AMSTAR tool.³⁷

Two senior investigators will independently assess each included study, with disagreements between assessors resolved through discussion to reach consensus. From our scan of the literature, we anticipate that the bulk of the literature will consist of case series. While case series are typically considered poor quality, we will complete quality assessments to inform our commentary on the relative merits of or caveats related to each study. We will retain poor-quality studies as part of the evidence base.

E. Data Synthesis

1. Preparing evidence tables. We will enter data into evidence tables by using predetermined abbreviations and acronyms consistently across all entries. The dimensions (i.e., areas of special focus, or the columns) of each evidence table may vary by KQ as appropriate, but the tables will contain some common elements, such as author, year of publication, population and intervention descriptions, sample size, key outcomes, and study type (e.g., randomized controlled trial, prospective observational study, etc.).

2. Synthesizing results. Given that the bulk of the research on feeding interventions for CP consists of case series, we anticipate largely qualitative synthesis of findings. As we

assess the literature, we will determine the potential for developing meta-analyses based on adequate and appropriately similar literature in terms of study design and outcomes.

Within each KQ, we will organize results by study design, with a focus on those designs less subject to bias (i.e., randomized controlled trials, controlled trials), those studies rated as having higher quality in our quality assessment process, and those employing comparison groups. Based on TEP input, we plan to stratify results of studies related to reflux outcomes by diagnostic technique (pH monitoring vs. impedance) where possible. Impedance is a newer and more valid technique that is not likely to be frequently reported in the literature to date.

F. Grading the Strength of Evidence for Individual Outcomes

We will use explicit criteria for rating the overall strength of the evidence for each key intervention-outcome pair for which the overall risk of bias is not overwhelmingly high. We will use established concepts of the quantity of evidence (e.g., numbers of studies, aggregate ending-sample sizes), the quality of evidence (from the quality ratings on individual articles), and the coherence or consistency of findings across similar and dissimilar studies and in comparison to known or theoretically sound ideas of clinical or behavioral knowledge. We will make these judgments as appropriate for each of the KQs.

The strength of evidence evaluation will be that stipulated in the Effective Health Care Program's *Methods Guide for Effectiveness and Comparative Effectiveness Reviews*,³⁴ which emphasizes the following four major domains: risk of bias (low, medium, high), consistency (inconsistency not present, inconsistency present, unknown or not applicable), directness (direct, indirect), and precision (precise, imprecise). Risk of bias is derived from the quality assessment of the individual studies that addressed the KQ and specific outcome under consideration. Each key outcome on each comparison of interest will be given an overall evidence grade based on the ratings for the individual domains.

The overall strength of evidence will be graded as “high” (indicating high confidence that the evidence reflects the true effect and further research is very unlikely to change our confidence in the estimate of effect), “moderate” (indicating moderate confidence that the evidence reflects the true effect and further research may change our confidence in the estimate of effect and may change the estimate), “low” (indicating low confidence that the evidence reflects the true effect and further research is likely to change our confidence in the estimate of effect and is likely to change the estimate), or “insufficient” (indicating that evidence is either unavailable or does not permit estimation of an effect). When no studies are available for an outcome or comparison of interest, we will grade the evidence as insufficient.

Two senior staff will independently grade the body of evidence; disagreements will be resolved as needed through discussion or third-party adjudication. We will record strength of evidence assessments in tables, summarizing for each outcome.

G. Assessing Applicability

We will assess the applicability of findings reported in the included literature to the general population of individuals with CP and feeding difficulties by determining the population, intervention, comparator, and setting in each study and developing an overview of these elements for each intervention category. We will also review potential modifiers of effect of

treatment to identify subgroups, which may include different age groups or levels of severity or functional status. We anticipate that participants in studies of surgical interventions likely have more severe feeding difficulties and are thus more selected than the general population. We also anticipate methodological heterogeneity in behavioral interventions such as caregiver training and variations in availability of some interventions.

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VI. Definition of Terms

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Published Online: June 12, 2012

- *Harms* are defined by the Evidence-based Practice Center Program as the totality of all possible adverse consequences of an intervention.
- We define *behavioral interventions* as including positioning, oral appliances, oral stimulation, sensorimotor facilitation, and caregiver training.
- We define *nutritional interventions* as food thickeners, caloric supplementation with formulas, vitamin supplementation, and altering food consistency.
- We define *significant reflux* as reflux requiring surgical or medical intervention.
- See also descriptions of severity and functionality classifications in Table 1.

VII. Summary of Protocol Amendments

In the event of protocol amendments, the date of each amendment will be accompanied by a description of the change and the rationale.

Example table below:

Date	Section	Original Protocol	Revised Protocol	Rationale

VIII. Review of Key Questions

For all EPC reviews, Key Questions were reviewed and refined as needed by the EPC with input from Key Informants and the Technical Expert Panel (TEP) to assure that the questions are specific and explicit about what information is being reviewed. In addition, for Comparative Effectiveness Reviews, the Key Questions were posted for public comment and finalized by the EPC after review of the comments.

IX. Key Informants

Key Informants are the end-users of research, including patients and caregivers, practicing clinicians, relevant professional and consumer organizations, purchasers of health care, and others with experience in making health care decisions. Within the EPC program, the Key Informant role is to provide input into identifying the Key Questions for research that will inform health care decisions. The EPC solicits input from Key Informants when developing questions for systematic review or when identifying high-priority research gaps and needed new research. Key Informants are not involved in analyzing the evidence or writing the report and have not reviewed the report, except as given the opportunity to do so through the peer or public review mechanism.

Key Informants must disclose any financial conflicts of interest greater than \$10,000 and any other relevant business or professional conflicts of interest. Because of their role as end-users, individuals are invited to serve as Key Informants and those who present with potential conflicts may be retained. The TOO and the EPC work to balance, manage, or mitigate any potential conflicts of interest identified.

X. Technical Experts

Technical Experts comprise a multidisciplinary group of clinical, content, and methodological experts who provide input in defining populations, interventions, comparisons, or outcomes, as well as identifying particular studies or databases to search. They are selected to provide broad expertise and perspectives specific to the topic under development. Divergent and conflicted opinions are common and perceived as healthy scientific discourse that results in a thoughtful, relevant systematic review. Therefore study questions, design, and/or methodological approaches do not necessarily represent the views of individual technical and content experts. Technical Experts provide information to the EPC to identify literature search strategies and recommend approaches to specific issues as requested by the EPC. Technical Experts do not do analysis of any kind nor contribute to the writing of the report and have not reviewed the report, except as given the opportunity to do so through the public review mechanism.

Technical Experts must disclose any financial conflicts of interest greater than \$10,000 and any other relevant business or professional conflicts of interest. Because of their unique clinical or content expertise, individuals are invited to serve as Technical Experts and those who present with potential conflicts may be retained. The TOO and the EPC work to balance, manage, or mitigate any potential conflicts of interest identified.

XI. Peer Reviewers

Peer reviewers are invited to provide written comments on the draft report based on their clinical, content, or methodological expertise. Peer review comments on the preliminary draft of the report are considered by the EPC in preparation of the final draft of the report. Peer reviewers do not participate in writing or editing of the final report or other products. The synthesis of the scientific literature presented in the final report does not necessarily represent the views of individual reviewers. The dispositions of the peer review comments are documented and will, for CERs and Technical Briefs, be published 3 months after the publication of the Evidence report.

Potential Reviewers must disclose any financial conflicts of interest greater than \$10,000 and any other relevant business or professional conflicts of interest. Invited Peer Reviewers may not have any financial conflict of interest greater than \$10,000. Peer reviewers who disclose potential business or professional conflicts of interest may submit comments on draft reports through the public comment mechanism.

XII. EPC Team Disclosures

We have no disclosures to note for any member of the team.

XIII. Role of the Funder

This project was funded under Contract No. xxx-xxxx-xxxxx from the Agency for Healthcare Research and Quality, U.S. Department of Health and Human Services. The Task Order Officer reviewed contract deliverables for adherence to contract requirements and quality. The authors of this report are responsible for its content. Statements in the report should not be construed as endorsement by the Agency for Healthcare Research and Quality or the U.S. Department of Health and Human Services.

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APPENDIX A. Exact Search Strings and Results

Table 1: PubMed search strategies (pubmed.gov interface) (updates search strategies on May 10, 2012)

Search terms	Preliminary search results
#1 "Neurologic Manifestations"[Mesh:NoExp] OR "Neuromuscular Manifestations"[mh] OR (neurologic*[tiab] AND (impairment*[tiab] OR impaired[tiab] OR problem*[tiab] OR deficit*[tiab]))	90,519
#2 ("Surgical Procedures, Operative"[MeSH] OR surgery[tiab] OR gastrostomy[tiab] OR "gastrostomy"[MeSH] OR "PEG tube"[tiab] OR "tube feeding"[tiab] OR "tube fed"[tiab] OR "tube-fed"[tiab] OR "G-tube"[tiab] OR "G tube"[tiab] OR "J-tube"[tiab] OR "J tube"[tiab] OR "gj tube"[tiab] OR "g-j tube"[tiab] OR "gastrostomy-jejunostomy tube"[tiab] OR "Jejunostomy"[Mesh] OR jejunostomy[tiab] OR gastrojejunostomy[tiab] OR "nasogastric tube"[tiab] OR "ng tube"[tiab] OR "nasogastric feeding"[tiab] OR "Enteral Nutrition"[mesh] OR "enteral feeding"[tiab] OR "enteral nutrition"[tiab] OR "Fundoplication"[mesh] OR fundoplication[tiab] OR antireflux[tiab] OR "Gastroesophageal Reflux/surgery"[Mesh] OR (reflux[tiab] AND (surgery[tiab] OR surgical[tiab]))	2,481,056
#3 ("Nutritional Support"[MeSH] OR "Nutritional Status"[MeSH] OR Eating[MeSH] OR "Deglutition disorders"[MeSH] OR feeding[tiab] OR nutrition[tiab] OR nutritional[tiab] OR eating[tiab] OR "Energy Intake"[mesh] OR "Feeding Behavior"[MH])	460,024
#4 #1 AND #2 AND #3 AND english[la]	720
#5 #3 AND editorial[pt]	0
#6 #3 AND letter[pt]	4
#7 #3 AND comment[pt]	3
#8 #3 AND case reports[pt]	142
#9 #3 AND review[pt]	95
#10 #3 AND news[pt]	0
#11 #3 AND guideline[pt]	1
#12 #3 AND practice guideline[pt]	1
#13 #3 AND historical article[pt]	0
#14 #3 AND jsubsetk	0
#15 #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14	228
#16 #4 NOT #15	492

Key: [mh] medical subject heading; [sh] subheading; [tiab] keyword in title or abstract; [la] language; [pt] publication type; jsubsetk consumer health subset; [PDAT] publication date.

* numbers may not add up as some records are indexed in multiple publication types.

Table 1: PubMed search strategies (pubmed.gov interface) (search last updated March 9, 2012)

Search terms	Preliminary search results
#1 ("Cerebral Palsy/drug therapy"[MeSH] OR "Cerebral Palsy/surgery"[MeSH] OR "Cerebral Palsy/diet therapy"[MeSH] OR "Cerebral Palsy/therapy"[MeSH]) OR ("cerebral palsy"[MeSH] OR "cerebral palsy"[tiab]) AND ("Surgical Procedures, Operative"[MeSH] OR surgery[tiab] OR "Drug Therapy"[MeSH] OR "drug"[tiab] OR "pharmacotherapy"[tiab] OR gastrostomy[tiab] OR "gastrostomy"[MeSH] OR "PEG tube"[tiab] OR "tube feeding"[tiab] OR "tube fed"[tiab] OR "tube-fed"[tiab] OR "G-tube"[tiab] OR "G tube"[tiab] OR "J-tube"[tiab] OR "J tube"[tiab] OR "gj tube"[tiab] OR "g-j tube"[tiab] OR "gastrostomy-jejunosomy tube"[tiab] OR "Jejunostomy"[Mesh] OR jejunostomy[tiab] OR gastrojejunostomy[tiab] OR "nasogastric tube"[tiab] OR "ng tube"[tiab] OR "nasogastric feeding"[tiab] OR "Enteral Nutrition"[mesh] OR "enteral feeding"[tiab] OR "enteral nutrition"[tiab] OR "Orthodontic Appliances"[MeSH] OR "intraoral appliance"[tiab] OR "intraoral appliances"[tiab] OR "oral appliance"[tiab] OR "oral appliances"[tiab] OR sensorimotor[tiab] OR "Feedback, Sensory"[mesh] OR "Posture"[mesh] OR posture[tiab] OR positioning[tiab] OR position[tiab] OR "Patient Positioning"[mesh] OR "Food, Fortified"[mesh] OR "Food, Formulated"[mesh] OR "Food Additives"[mesh] OR (food[tiab] OR "Food"[mesh]) AND (handling[tiab] OR thickness[tiab] OR thickener*[tiab] OR consistency[tiab] OR additive[tiab] OR texture*[tiab] OR composition[tiab] OR presentation[tiab] OR preparation[tiab])) OR "ThickenUp"[tiab] OR "Thick-It"[tiab] OR SimplyThick[tiab] OR "Thick and Easy"[tiab] OR "feeding device"[tiab] OR "feeding devices"[tiab] OR "Self-Help Devices"[mesh] OR "Occupational Therapy"[mesh] OR "occupational therapy"[tiab] OR "Behavior Therapy"[mesh] OR "behavior therapy"[mesh] OR "behavioral therapy"[tiab] OR "Fundoplication"[mesh] OR fundoplication[tiab] OR antireflux[tiab] OR "Gastroesophageal Reflux/surgery"[Mesh] OR (reflux[tiab] AND (surgery[tiab] OR surgical[tiab])) OR "Family Therapy"[mesh] OR "family therapy"[tiab] OR ("Parenting"[mesh] OR parent*[tiab] OR family[tiab] OR caregiver*[tiab] OR Caregivers[mesh]) AND (behavior*[tiab] OR therapy[tiab] OR intervention*[tiab]))))	8,070
#2 ("Nutritional Support"[MeSH] OR "Nutritional Status"[MeSH] OR Eating[MeSH] OR "Deglutition disorders"[MeSH] OR feeding[tiab] OR nutrition[tiab] OR nutritional[tiab] OR eating[tiab] OR "Energy Intake"[mesh] OR "Feeding Behavior"[MH])	455,518
#3 #1 AND #2 AND english[la]	353
#4 #3 AND editorial[pt]	2
#5 #3 AND letter[pt]	2
#6 #3 AND comment[pt]	7
#7 #3 AND case reports[pt]	54
#8 #3 AND review[pt]	49
#9 #3 AND news[pt]	1
#10 #3 AND guideline[pt]	1
#11 #3 AND practice guideline[pt]	0
#12 #3 AND meta-analysis[pt]	1
#13 #3 AND historical article[pt]	1
#14 #3 AND jsubsetk	0
#15 #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14	109
#16 #3 NOT #15	244

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Published Online: June 12, 2012

#17	#16 AND ("1980"[PDAT] : "3000"[PDAT]) [limits to 1980 to present]	222
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Key: [mh] medical subject heading; [sh] subheading; [tiab] keyword in title or abstract; [la] language; [pt] publication type; jsubsetk consumer health subset; [PDAT] publication date.

* numbers may not add up as some records are indexed in multiple publication types.

Table 1: PsycINFO search strategies (ProQuest CSA Illumina interface) (search last updated March 9, 2012)

Search terms	Preliminary search results
#1 ((KW="cerebral palsy") AND (KW="surgery" OR KW="drug therapy" OR KW="Drug" OR KW="Pharmacotherapy" OR KW="gastrostomy" OR KW="Gastrojejunostomy" OR KW="Gastrojejunostomy tube" OR KW="PEG Tube" OR KW="tube feeding" OR KW="tube fed" OR KW="G tube" OR KW="G-Tube" OR KW="J tube" OR KW="J-Tube" OR KW="GJ Tube" OR KW="G-J Tube" OR KW="Gastrostomy-jejunostomy tube" OR KW="Jejunostomy" OR KW="nasogastric tube" OR KW="ng tube" OR KW="nasogastric feeding" OR KW="orthodontic appliance*" OR KW="intraoral appliance*" OR KW="oral appliance*" OR KW="sensorimotor" OR KW="Sensory Feedback" OR KW="Feedback" OR KW="Posture" OR KW="Positioning" OR KW="Position*" OR (KW="Food" AND (KW="handling" OR KW="Thickness" OR KW="thickener*" OR KW="Consistency" OR KW="Additive*" OR KW="Texture*" OR KW="Composition*" OR KW="Presentation" OR KW="Preparation*")) OR KW="Food Additive" OR KW="Food Additives" OR KW="Feeding device" OR KW="Feeding devices" OR KW="Self-help device*" OR KW="Assistive Technology Devices" OR KW="Assistive Technology" OR KW="Assistive Devices" OR KW="Occupational Therapy" OR KW="Behavioral Therapy" OR KW="Behavior Therapy" OR KW="Behavior Modification" OR KW="Behavior" OR KW="Fundoplication" OR KW="Gastric Fundus" OR KW="Antireflux" OR (KW="Reflux" AND (KW="Surgery OR KW="Surgical")) OR KW="Family Therapy" OR KW="Family counseling" OR KW="Psychotherapeutic Counseling" OR KW="Parent Training" OR ((KW="Family OR KW="Parent*" OR KW="Caregivers" OR KW=caregiver) AND (KW="Behavior" OR KW="Therapy" OR KW="Intervention*"))))	1,159
#2 KW="Nutrition" OR KW="Eating" OR KW="Feeding" OR KW="Intake" OR KW="Nutritional" OR KW="Eating Behavior" OR KW="Feeding Behavior" OR KW="food" OR KW="Food Intake"	110,030
#3 #1 AND #2 AND "English"	80
#4 #3 AND <ul style="list-style-type: none"> • Limited to Journals 	70
#5 #4 limited to 1980 to 2012	62

Key: KW Keyword; it was not possible to exclude MEDLINE citations, so these may overlap with those findings

Table 1: CINAHL search strategies (EBSCOhost interface) (search last updated March 9, 2012)

Search terms	Preliminary search results
#1 (MH "Cerebral Palsy/DT/SU/DH/TH OR ((MH "Cerebral Palsy" OR TX "Cerebral Palsy") AND ((MH "Surgery, Operative+" OR TX "Surgery" OR MH "Drug Therapy+" OR TX "Drug" OR TX "Pharmacotherapy" OR TX "Gastrostomy" OR MH "Gastrostomy" OR MH "Gastrojejunostomy Tubes+" OR TX "PEG tube" OR TX "tube feeding" OR TX "tube fed" OR TX "tube-fed" OR TX "G-tube" OR TX "G tube" OR TX "J-tube" OR TX "J tube" OR TX "gj tube" OR TX "g-j tube" OR TX "gastrostomy-jejunostomy tube" OR MH "Jejunostomy" OR TX "jejunostomy" OR TX "gastrojejunostomy" OR TX "nasogastric tube" OR TX "ng tube" OR TX "nasogastric feeding") OR (MH "Enteral Nutrition" OR TX "enteral feeding" OR TX "enteral nutrition") OR (MH "Orthodontic Appliances" OR TX "intraoral appliance" OR TX "intraoral appliances" OR TX "oral appliance" OR TX "oral appliances") OR (TX "sensorimotor" OR TX "Sensory feedback" OR MH "Feedback" OR MH "Posture+" OR TX "posture" OR TX "positioning" OR TX "position" OR MH "Patient Positioning+") OR MH "Food Additives" OR MH "Food, Formulated" OR MH "Food, Fortified" OR ((TX "food" OR MH "Food+") AND (TX "handling" OR TX "thickness" OR thickener* OR TX "consistency" OR TX "additive*" OR TX "texture*" OR TX "composition" OR TX "presentation" OR preparation*)) OR TX "ThickenUP" OR TX "Thick-IT" OR TX "SimplyThick" OR TX "Thick and Easy" OR TX "feeding device" OR TX "feeding devices" OR TX "Self-Help Devices" OR MH "Assistive Technology Devices+" OR MH "Occupational Therapy+" OR TX "occupational therapy" OR MH "Behavior Modification+" OR MH "Behavior Therapy+" OR TX "behavior therapy" OR TX "behavioral therapy" OR TX "Fundoplication" OR MH "Gastric Fundus/SU" OR TX "antireflux" OR MH "Gastroesophageal Reflux/SU" OR (TX "reflux" AND (TX "surgery" OR TX "surgical"))) OR MH "Family Therapy" OR TX "family therapy" OR ((MH "Parenting" OR parent* OR TX "family" OR MH "Caregivers" OR TX "caregiver*") AND (TX "behavior*" OR TX "therapy" OR TX "intervention*"))))	2,461
#2 (MH "Nutritional Support+" OR MH "Home Nutritional Support" OR MH "Nutritional Status" OR MH "Nutrition (Iowa NOC) (Non-Cinch)+" OR MH "Eating" OR MH "Deglutition disorders" OR TX "feeding" OR TX "nutrition" OR TX "nutritional" OR TX "eating" OR MH "Energy Intake" OR MH "Eating Behavior" OR TX "Feeding behavior")	135,253
#3 S1 AND S2 AND LA "English"	208
#4 S3 AND PT "editorial"	0
#5 S3 AND PT "letter"	0
#6 S3 AND PT "commentary"	6
#7 S3 AND PT "case study"	20
#8 S3 AND PT "review"	18
#9 S3 AND PT "practice guidelines"	1
#10 S3 AND PT "meta analysis"	0
#11 S3 AND PT "historical material"	0
#12 S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11	45
#13 S3 NOT S12 • Excluding MEDLINE	163 71
#14 Published Date from: 19800101-30001231; [limits 1980-present]	71

Key: MH CINAHL Subject Headings; + Explode Search Term; TX All Text; LA Language; PT Publication Type
* numbers may not add up as some records are indexed in multiple publication types.

Table 1: ERIC search strategies (eric.ed.gov interface) (search last updated March 9, 2012)

Search terms		Preliminary search results
#1	(Keywords:cerebral and Keywords:palsy)	1,191
#2	(Keywords:eating OR Keywords:feeding OR Keywords:nutrition OR Keywords:food OR Keywords:nutritional)	21,419
#3	((Keywords:cerebral and Keywords:palsy) and (Keywords:eating OR Keywords:feeding OR Keywords:nutrition OR Keywords:food OR Keywords:nutritional)) and (Publication Type:"Journal Articles"), Publication Date:1980-2012	16

Key: [mh] medical subject heading; [sh] subheading; [tiab] keyword in title or abstract; [la] language; [pt] publication type; jsubsetk consumer health subset; [dp] publication date.

* numbers may not add up as some records are indexed in multiple publication types.

It was not possible to exclude MEDLINE citations, so these may overlap with those findings.

Table 1: REHABDATA search strategies (<http://www.naric.com/research/rehab/> interface) (search last updated March 9, 2012)

Search terms		Preliminary search results
#1	Exact Phrase: cerebral palsy + At Least One of: eating food feeding nutrition nutritional – limited to 1980-2012	32
#2	Hand-limited to exclude items that are clearly books or from non-research periodicals	21

Used the advanced search interface for REHABDATA;

<http://www.naric.com/research/rehab/results.cfm?search=2&type=advanced&all=&exact=cerebral%20palsy&any=eating%20food%20feeding%20nutrition%20nutritional&omit=&fld1=Title&txt1=&op1=AND&fld2=Title&txt2=&op2=AND&fld3=Title&txt3=&op3=AND&fld4=Title&txt4=&dte1=1980&dte2=2012&available=0&online=0>

It was not possible to exclude MEDLINE citations, so these may overlap with those findings

Table 1: OTseeker search strategies (www.otseeker.com interface) (search last updated March 8, 2012)

Search terms		Preliminary search results
#1	"cerebral palsy" AND (eating OR feeding OR nutrition OR nutritional OR food) AND Year Published: 1980 -	5

It was not possible to exclude MEDLINE citations, so these may overlap with those findings.

APPENDIX B. Tools used to Assess Methodological Risk of Bias of Individual Studies

Cochrane Collaboration modified tool for assessing risk of bias for RCT's, PART I

Use this form to assess risk of bias for randomized controlled trials.

Bias is assessed as a judgment (high, low, or unclear) for individual elements from five domains of bias (selection, performance, attrition, reporting, and other).

Risk of selection, reporting, and other bias are assessed in the **Quality Assessment Form Part I**. Risk of performance, detection, and attrition bias are assessed using the **Quality Assessment Form Part II**.

Using the guidance provided at the end of this form, select either "high", "low" or "unclear" for each judgment. When complete, proceed to **Part II of the Quality Assessment Form**

REF ID:					
<i>Domain</i>	<i>Description</i>	<i>High risk of bias</i>	<i>Low risk of bias</i>	<i>Unclear risk of bias</i>	<i>Reviewer Assessment</i>
<i>Selection bias</i> Random sequence generation	Described the method used to generate the allocation sequence in sufficient detail to allow an assessment of whether it should produce comparable groups. Reviewer Comments:	Selection bias (biased allocation to interventions) due to inadequate generation of a randomized sequence.	Random sequence generation method should produce comparable groups	Not described in sufficient detail	Judgment: Random sequence generation <input type="checkbox"/> High <input type="checkbox"/> Low <input type="checkbox"/> Unclear
<i>Selection bias</i> Allocation concealment	Described the method used to conceal the allocation sequence in sufficient detail to determine whether intervention allocations could have been foreseen in advance of, or during, enrollment. Reviewer Comments:	Selection bias (biased allocation to interventions) due to inadequate concealment of allocations prior to assignment.	Intervention allocations likely could not have been foreseen in advance of, or during, enrollment	Not described in sufficient detail	Judgment: Allocation concealment <input type="checkbox"/> High <input type="checkbox"/> Low <input type="checkbox"/> Unclear
<i>Domain</i>	<i>Description</i>	<i>High risk of bias</i>	<i>Low risk of bias</i>	<i>Unclear risk of bias</i>	<i>Reviewer Assessment</i>
<i>Reporting Bias</i> Selective	State how the possibility of selective outcome reporting was examined by the authors and what was found.	Reporting bias due to selective outcome reporting.	Selective outcome reporting bias not detected	Insufficient information to permit judgment of 'Low risk' or 'High risk'.	Judgment: Selective reporting <input type="checkbox"/> High



reporting	Reviewer Comments:			<i>(It is likely that the majority of studies will fall into this category.)</i>	<input type="checkbox"/> Low <input type="checkbox"/> Unclear
Other bias Other sources of bias	Any important concerns about bias not addressed above. If particular questions/entries were pre-specified in the study's protocol, responses should be provided for each question/entry. Reviewer Comments:	Bias due to problems not covered elsewhere in the table.	No other bias detected	There may be a risk of bias, but there is either: Insufficient information to assess whether an important risk of bias exists; or Insufficient rationale or evidence that an identified problem will introduce bias.	Judgment: Other sources of bias <input type="checkbox"/> High <input type="checkbox"/> Low <input type="checkbox"/> Unclear

Cochrane Collaboration modified tool for assessing risk of bias for RCT's, PART II

Use this form to assess risk of bias for randomized controlled trials.

Bias is assessed as a judgment (high, low, or unclear) for individual elements from five domains of bias (selection, performance, attrition, reporting, and other).

Risk of selection, reporting, and other bias are assessed in the **Quality Assessment Form Part I**. Risk of performance, detection, and attrition bias are assessed using the **Quality Assessment Form Part II**.

Using the guidance provided at the end of this form, select either "high", "low" or "unclear" for each judgment.

Risk of bias for the domains in the Form Part II will be assessed for each main or class of outcomes. Please indicate the specific outcome and complete the assessment for each.

REF ID:					
Outcome(s):					
Domain	Description	High risk of bias	Low risk of bias	Unclear risk of bias	Reviewer Assessment
<i>Performance bias</i> Blinding (participants and personnel)	Described all measures used, if any, to blind study participants and personnel from knowledge of which intervention a participant received. Provided any information relating to whether the intended blinding was effective. Reviewer Comments:	Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.	Blinding was likely effective.	Not described in sufficient detail	Judgment: Blinding (participants and personnel) <input type="checkbox"/> High <input type="checkbox"/> Low <input type="checkbox"/> Unclear
<i>Detection bias</i> Blinding (outcome assessment)	Described all measures used, if any, to blind outcome assessors from knowledge of which intervention a participant received. Provided any information relating to whether the intended blinding was effective. Reviewer Comments:	Detection bias due to knowledge of the allocated interventions by outcome assessors.	Blinding was likely effective.	Not described in sufficient detail	Judgment: Blinding (outcome assessment) <input type="checkbox"/> High <input type="checkbox"/> Low <input type="checkbox"/> Unclear

Domain	Description	High risk of bias	Low risk of bias	Unclear risk of bias	Reviewer Assessment
<p><i>Attrition bias</i></p> <p>Incomplete outcome data</p>	<p>Described the completeness of outcome data for each main outcome, including attrition and exclusions from the analysis. Stated whether attrition and exclusions were reported, the numbers in each intervention group (compared with total randomized participants), reasons for attrition/exclusions where reported.</p> <p>Reviewer Comments:</p>	<p>Attrition bias due to amount, nature or handling of incomplete outcome data.</p>	<p>Handling of incomplete outcome data was complete and unlikely to have produced bias</p>	<p>Insufficient reporting of attrition/exclusions to permit judgment of 'Low risk' or 'High risk' (e.g. number randomized not stated, no reasons for missing data provided)</p>	<p>Judgment: Incomplete outcome data</p> <p><input type="checkbox"/> High</p> <p><input type="checkbox"/> Low</p> <p><input type="checkbox"/> Unclear</p>

Newcastle-Ottawa Quality Assessment Form for Cohort Studies

Note: A study can be given a maximum of one star for each numbered item within the Selection and Outcome categories. A maximum of two stars can be given for Comparability.

REFID: _____

Reviewer: _____

Selection

- 1) Representativeness of the exposed cohort
 - a) Truly representative (**one star**)
 - b) Somewhat representative (**one star**)
 - c) Selected group
 - d) No description of the derivation of the cohort
- 2) Selection of the non-exposed cohort
 - a) Drawn from the same community as the exposed cohort (**one star**)
 - b) Drawn from a different source
 - c) No description of the derivation of the non exposed cohort
- 3) Ascertainment of exposure
 - a) Secure record (e.g., surgical record) (**one star**)
 - b) Structured interview (**one star**)
 - c) Written self report
 - d) No description
 - e) Other
- 4) Demonstration that outcome of interest was not present at start of study
 - a) Yes (**one star**)
 - b) No

Comparability

- 1) Comparability of cohorts on the basis of the design or analysis controlled for confounders
 - a) The study controls for age (**one star**)
 - b) Study controls for other factors (list) _____ (**one star**)
 - c) Cohorts are not comparable on the basis of the design or analysis controlled for confounders

Outcome

- 1) Assessment of outcome
 - a) Independent blind assessment (**one star**)
 - b) Record linkage (**one star**)
 - c) Self report
 - d) No description
 - e) Other
- 2) Was follow-up long enough for outcomes to occur
 - a) Yes (**one star**)
 - b) No

Indicate the median duration of follow-up and a brief rationale for the assessment above: _____

- 3) Adequacy of follow-up of cohorts
 - a) Complete follow up- all subject accounted for (**one star**)
 - b) Subjects lost to follow up unlikely to introduce bias- number lost less than or equal to 20% or description of those lost suggested no different from those followed. (**one star**)
 - c) Follow up rate greater than 80% and no description of those lost
 - d) No statement

Newcastle-Ottawa Quality Assessment Form for Case-control Studies

Note: A study can be given a maximum of one star for each numbered item within the Selection and Exposure categories. A maximum of two stars can be given for Comparability.

REFID: _____

Reviewer: _____

Selection

- 1) Is the case definition adequate?
 - a) Yes, with independent validation (**one star**)
 - b) Yes, e.g., record linkage or based on self report
 - c) No description
- 2) Representativeness of the cases
 - a) Consecutive or obviously representative series of cases (**one star**)
 - b) Potential for selection biases or not stated
- 3) Selection of controls
 - a) Community controls (**one star**)
 - b) Hospital controls
 - c) No description
- 4) Definition of controls
 - a) No history of disease (endpoint) (**one star**)
 - b) No description of source

Comparability

- 1) Comparability of cases and controls on the basis of the design or analysis controlled for confounders
 - The study controls for age (**one star**)
 - Study controls for other factors (list) _____ (**one star**)
 - Cohorts are not comparable on the basis of the design or analysis controlled for confounders

Exposure

- 1) Ascertainment of exposure
 - a) Secure record (e.g., surgical record) (**one star**)
 - b) Structured interview where blind to case/control status (**one star**)
 - c) Interview not blinded to case/control status
 - d) Written self report or medical record only
 - e) No description
- 2) Same method of ascertainment for cases and controls
 - Yes (**one star**)
 - No
- 3) Non-response rate
 - a) Same rate for both groups (**one star**)
 - b) Non-respondents described
 - c) Rate different between cases and controls with no description

Minimum criteria to assess risk of bias in case series

Risk of Bias	Criterion	Yes/No/Unclear
Selection bias and confounding	Were the important confounding and modifying variables taken into account in the design and analysis?	

Risk of Bias	Criterion	Yes/No/Unclear
Performance bias	Did researchers rule out any impact from a concurrent intervention or an unintended exposure that might bias results?	
	Did variation from the study protocol compromise the conclusions of the study?	
Attrition bias	Was there a high rate of differential or overall attrition?	
	Did attrition result in a difference in group characteristics between baseline (or randomization) and follow-up?	
Detection bias	Were the outcome assessors blinded to the intervention or exposure status of participants?	
	Are the inclusion/exclusion criteria measured using valid and reliable measures, implemented consistently across all study participants?	
	Are interventions/exposures assessed using valid and reliable measures, implemented consistently across all study participants?	
	Are primary outcomes assessed using valid and reliable measures, implemented consistently across all study participants?	
	Are confounding variables assessed using valid and reliable measures, implemented consistently across all study participants?	
	Did the study account for secular trends and regression to the mean?	
Reporting bias	Are the potential outcomes, including harms, pre-specified by the researchers?	
	Are all pre-specified outcomes reported?	

AMSTAR Tool for Systematic Reviews

<p>1. Was a <i>a priori</i> design provided? The research question and inclusion criteria should be established before the conduct of the review.</p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Can't answer <input type="checkbox"/> Not applicable</p>
<p>2. Was there duplicate study selection and data extraction? There should be at least two independent data extractors and a consensus procedure for disagreements should be in place.</p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Can't answer <input type="checkbox"/> Not applicable</p>
<p>3. Was a comprehensive literature search performed? At least two electronic sources should be searched. The report must include years and databases used (e.g. Central, EMBASE, and MEDLINE). Key words and/or MESH terms must be stated and where feasible the search strategy should be provided. All searches should be supplemented by consulting current contents, reviews, textbooks, specialized registers, or experts in the particular field of study, and by reviewing the references in the studies found.</p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Can't answer <input type="checkbox"/> Not applicable</p>
<p>4. Was the status of publication (i.e. grey literature) used as an inclusion criterion? The authors should state that they searched for reports regardless of their publication type. The authors should state whether or not they excluded any reports (from the systematic review), based on their publication status, language etc.</p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Can't answer <input type="checkbox"/> Not applicable</p>
<p>5. Was a list of studies (included and excluded) provided? A list of included and excluded studies should be provided.</p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Can't answer <input type="checkbox"/> Not applicable</p>
<p>6. Were the characteristics of the included studies provided? In an aggregated form such as a table, data from the original studies should be provided on the participants, interventions and outcomes. The ranges of characteristics in all the studies analyzed e.g. age, race, sex, relevant socioeconomic data, disease status, duration, severity, or other diseases should be reported.</p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Can't answer <input type="checkbox"/> Not applicable</p>
<p>7. Was the scientific quality of the included studies assessed and documented? A priori' methods of assessment should be provided (e.g., for effectiveness studies if the author(s) chose to include only randomised, double-blind, placebo controlled studies, or allocation concealment as inclusion criteria); for other types of studies alternative items will be relevant.</p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Can't answer <input type="checkbox"/> Not applicable</p>
<p>8. Was the scientific quality of the included studies used appropriately in formulating conclusions? The results of the methodological rigor and scientific quality should be considered in the analysis and the conclusions of the review, and explicitly stated in formulating recommendations.</p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Can't answer <input type="checkbox"/> Not applicable</p>
<p>9. Were the methods used to combine the findings of studies appropriate? For the pooled results, a test should be done to ensure the studies were combinable, to assess their homogeneity (i.e. Chi-squared test for homogeneity, I₂). If heterogeneity exists a random effects model should be used and/or the clinical appropriateness of combining should be taken into consideration (i.e. is it sensible to combine?).</p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Can't answer <input type="checkbox"/> Not applicable</p>

<p>10. Was the likelihood of publication bias assessed? An assessment of publication bias should include a combination of graphical aids (e.g., funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test).</p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Can't answer <input type="checkbox"/> Not applicable</p>
<p>11. Was the conflict of interest included? Potential sources of support should be clearly acknowledged in both the systematic review and the included studies.</p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Can't answer <input type="checkbox"/> Not applicable</p>