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Early Intervention for Children Aged 0 to 2 Years With or at High Risk of Cerebral Palsy International Clinical Practice Guideline Based on Systematic Reviews

Morgan, Catherine; Feters, Linda; Adde, Lars; Badawi, Nadia; Bancale, Ada; Boyd, Roslyn N.; Chorna, Olena; Cioni, Giovanni; Damiano, Diane L.; Darrah, Johanna

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Early Intervention for Children Aged 0 to 2 Years With or at High Risk of Cerebral Palsy

International Clinical Practice Guideline Based on Systematic Reviews

Catherine Morgan, PhD; Linda Fetters, PhD; Lars Adde, PhD; Nadia Badawi, PhD; Ada Bancale, NPT; Roslyn N. Boyd, PhD; Olena Chorna, CCRP; Giovanni Cioni, MD; Diane L. Damiano, PhD; Johanna Darrah, PhD; Linda S. de Vries, PhD; Stacey Dusing, PhD; Christa Einspieler, PhD; Ann-Christin Eliasson, PhD; Donna Ferriero, MD; Darcy Fehlings, MD; Hans Forssberg, MD; Andrew M. Gordon, PhD; Susan Greaves, PhD; Andrea Guzzetta, PhD; Mijna Hadders-Algra, PhD; Regina Harbourne, PhD; Petra Karlsson, PhD; Lena Krumlinde-Sundholm, PhD; Beatrice Latal, PhD; Alison Loughran-Fowlds, PhD; Catherine Mak, PhD; Nathalie Maitre, MD; Sarah McIntyre, PhD; Cristina Mei, PhD; Angela Morgan, PhD; Angelina Kakooza-Mwesige, PhD; Domenico M. Romeo, PhD; Katherine Sanchez, PhD; Alicia Spittle, PhD; Roberta Shepherd, PhD; Marelle Thornton, DipEd; Jane Valentine, PhD; Roslyn Ward, PhD; Koa Whittingham, PhD; Alieh Zamany, DPT; Iona Novak, PhD

IMPORTANCE Cerebral palsy (CP) is the most common childhood physical disability. Early intervention for children younger than 2 years with or at risk of CP is critical. Now that an evidence-based guideline for early accurate diagnosis of CP exists, there is a need to summarize effective, CP-specific early intervention and conduct new trials that harness plasticity to improve function and increase participation. Our recommendations apply primarily to children at high risk of CP or with a diagnosis of CP, aged 0 to 2 years.

OBJECTIVE To systematically review the best available evidence about CP-specific early interventions across 9 domains promoting motor function, cognitive skills, communication, eating and drinking, vision, sleep, managing muscle tone, musculoskeletal health, and parental support.

EVIDENCE REVIEW The literature was systematically searched for the best available evidence for intervention for children aged 0 to 2 years at high risk of or with CP. Databases included CINAHL, Cochrane, Embase, MEDLINE, PsycInfo, and Scopus. Systematic reviews and randomized clinical trials (RCTs) were appraised by A Measurement Tool to Assess Systematic Reviews (AMSTAR) or Cochrane Risk of Bias tools. Recommendations were formed using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) framework and reported according to the Appraisal of Guidelines, Research, and Evaluation (AGREE) II instrument.

FINDINGS Sixteen systematic reviews and 27 RCTs met inclusion criteria. Quality varied. Three best-practice principles were supported for the 9 domains: (1) immediate referral for intervention after a diagnosis of high risk of CP, (2) building parental capacity for attachment, and (3) parental goal-setting at the commencement of intervention. Twenty-eight recommendations (24 for and 4 against) specific to the 9 domains are supported with key evidence: motor function (4 recommendations), cognitive skills (2), communication (7), eating and drinking (2), vision (4), sleep (7), tone (1), musculoskeletal health (2), and parent support (5).

CONCLUSIONS AND RELEVANCE When a child meets the criteria of high risk of CP, intervention should start as soon as possible. Parents want an early diagnosis and treatment and support implementation as soon as possible. Early intervention builds on a critical developmental time for plasticity of developing systems. Referrals for intervention across the 9 domains should be specific as per recommendations in this guideline.

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Author Affiliations: Author affiliations are listed at the end of this article.

Corresponding Author: Iona Novak, PhD, University of Sydney, Level 7, Western Ave, D18-Susan Wakil Health Building, Sydney 2006, NSW, Australia (iona.novak@sydney.edu.au).

Cerebral palsy (CP) is the most common childhood physical disability. Variation in birth prevalence exists in high-income countries (1.4 to 2.5 affected children per 1000 live births) and is higher again in low- to middle-income countries.¹⁻⁵ Cerebral palsy occurs because of a lesion or maldevelopment in the developing brain. Often, the full causal pathway is unclear. Cerebral palsy is a clinical diagnosis of movement disorders, resulting in either spasticity (92%), dyskinesia (4%), ataxia (1%), hypotonia (not classified in all countries; 2%), or mixed types.² Dyskinesia, ataxia, and hypotonia typically affect all 4 limbs. Spasticity is categorized topographically, as unilateral (hemiplegia; 59%) or bilateral (including diplegia, with the lower limbs more affected than upper limbs [10%] and quadriplegia or tetraplegia, with 4 limbs and trunk affected [31%]).² Infants and children have remarkable brain plasticity and aptitude for learning; taking advantage of this window of opportunity with evidence-based intervention for those with early brain injury maximizes functional outcomes and minimizes complications. However, not all interventions are suitable for all children with CP, because age, type, topography, severity, parental variables, environmental variables, and principles of neuroplasticity drive the choice of best treatment.⁶ Co-occurring impairments and functional limitations are common (including pain [75%], epilepsy [35%], intellectual disability [49%], musculoskeletal deformities [eg, hip displacement; 28%], behavioral disorders [26%], sleep disorders [23%], and/or vision [11%] and hearing [4%] impairments⁷) and may have a greater effect on function and quality of life than motor impairment. Children with involvement in 4 limbs experience higher rates of comorbidities and worse outcomes (especially when epilepsy and intellectual disability are present),⁷ and conversely, children with involvement of fewer limbs and fewer comorbidities have better responses to intervention.

These guideline recommendations apply to children aged 0 to 2 years who are at high risk or have a diagnosis of CP, as defined in the 2017 diagnostic international guideline,⁸ but not infants born preterm without identifiable brain injury, since many of these infants will not have CP.⁹ To assign the interim clinical diagnosis of high risk of CP, the infant must have motor dysfunction (an essential criterion) and at least 1 of 2 additional criteria, namely abnormal neuroimaging or a clinical history indicating a risk for CP.⁸ We refer readers to the 2017 guideline⁸ for more detailed information regarding early and accurate diagnosis of CP.

Our objective was to develop clinical guidelines for early intervention (treatment and management) in children at high risk of CP and their families. This has been developed through a systematic review of the best available evidence for improving 9 domains in children aged 0 to 2 years with or at high risk of CP.

Methods

This guideline was developed using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) framework and the Appraisal of Guidelines, Research, and Evaluation (AGREE) II tool.¹⁰ Comprehensive systematic searches, using the Cochrane method, were conducted for the 9 topics within the target age range using Patient, Intervention, Comparison, and Outcome (PICO)¹¹ searches (eTable 1 in the [Supplement](#)). The inclusion criteria specified (1) gathering existing systematic reviews answer-

Key Points

Question What are the evidence-based recommendations to guide early intervention in children aged 0 to 2 years who have or are at high risk of cerebral palsy?

Findings In this systematic review, there was good-quality evidence for involvement of parents in intervention programs and task-specific and context-specific interventions to improve motor and cognitive outcomes in children with cerebral palsy. The evidence in other developmental domains is not as strong, and conditional recommendations are based on other high-risk populations.

Meaning It is critical that early intervention for cerebral palsy starts at diagnosis and the associated impairments are monitored and treated according to recommendations.

ing the PICO questions; (2) when systematic reviews were not available, conducting a new systematic review to identify randomized clinical trials (RCTs) or the best available lower levels of evidence when systematic reviews and RCTs were not available¹²; or (3) when no or limited data on CP in children aged 0 to 2 years were published, conducting searches to identify RCTs in patients with other neurodevelopmental disabilities or older children with CP ([Table](#)).

Topic literature was appraised by 9 domain-specific working groups using A Measurement Tool to Assess Systematic Reviews (AMSTAR)⁹⁷ for existing systematic reviews (eTable 2 in the [Supplement](#)) or the Cochrane Risk of Bias tool⁹⁸ for RCTs (eTable 3 in the [Supplement](#)). Groups summarized the certainty of supporting evidence and formulated recommendations using the GRADE evidence to decision framework (eTable 4 in the [Supplement](#)).⁹⁹ GRADE uses a 4-part continuum for recommendations, using the terms *strong for*, *conditional for*, *conditional against*, and *strong against*. We assessed (1) the balance between desirable and undesirable consequences of using different intervention strategies or not providing the intervention; (2) evidence quality; (3) family preferences, including benefits vs risks and inconvenience; and (4) costs.

The entire author panel reviewed the text, evidence tables, and supporting literature. Consensus agreement on recommendations arising from the appraised evidence was reached by discussion. Ratification of the final recommendations, including resolution of disagreements among coauthors, was completed by the lead authors (C.M., L.F., and I.N.).

Results

Sixteen systematic reviews and 25 RCTs met inclusion criteria of the 9 topics. Evidence quality was variable, and only a few strong recommendations are made ([Table](#); [Figure](#)). The [Table](#) and [Figure](#) indicate the population evidence source. The strongest of the 28 recommendations are derived from the literature on children younger than 2 years with or at risk for CP. Recommendations derived from infants born preterm, older children with CP or other neurological conditions, or infants and children developing typically were coded as conditional because they were downgraded for imprecision.

Table. Recommendations

No.	Domain	Strength	Direction	Intervention	Key recommendations	Target population
Skills development						
1	Motor	Strong	(1) For and (2) against	Early intervention	(1) We recommend beginning intervention at the time of suspected diagnosis ^{8,13} to harness neuroplasticity through specific training ^{8,13} and respecting parent requests for early intervention ^{14,15} and (2) we recommend against waiting and seeing because the critical window for neuromuscular plasticity is misused. ^{8,13}	Children with or at high risk of unilateral or bilateral CP
2	Motor	Strong	For	Task-specific motor training	We recommend task-specific motor training that includes self-discovery of the environment and solutions to overcome movement challenges, ¹⁶⁻²⁴ selection of challenging but achievable motor tasks that require persistence for success, ^{16,18,20-22,25,26} daily repeated practice (as possible) for skills acquisition and refinement, parental coaching to structure practice beyond scheduled therapy sessions (for adequate dosing), and creating enriched environments promoting movement variety and intense, enjoyable practice. ^{13,27,28}	Children with or at high risk of unilateral or bilateral CP
3	Motor	Strong	Against	Passive movement	We recommend against passive, therapist-controlled handling techniques for movement activation or activities. ^{6,17,29,30}	Children with or at high risk of unilateral or bilateral CP
4	Motor	Strong	For	CIMT or bimanual therapy	We recommend CIMT and/or bimanual training as soon as a unilateral CP diagnosis is suspected, since benefits outweigh the risk of harm from unused plasticity windows ^{8,13} and false-positive diagnoses. ^{22,31} We recommend short intervals of CIMT (30-60 min of therapist-supervised home programs for 6 wk) in early infancy, increasing in intensity with age. ^{31,32}	Children with unilateral CP
5	Cognitive	Strong	For	Cognitive intervention	We recommend targeted cognitive interventions, because motor impairment hampers social interactions and exploration of the environment and toys restricting discovery-based learning. ^{16,17,29} We recommend cognitive interventions that include active, self-initiated, self-generated movements of real tasks with observable consequences; social interaction with people and objects ^{19,33-35} ; multimodal learning (cognitive, language, and motor); challenging tasks with incremented complexity ^{16,19,36} ; parent participation ³⁷ ; and best-practice early-years enrichment (eg, adequate nutrition, interactive, child-led learning). ³⁸	Children with or at high risk of CP (all motor types)
6	Cognitive	Conditional	Against	Generic developmental education alone and/or with a sole focus on passive movement	We recommend against generic developmental education alone and/or a sole focus on motor development using passive motor interventions to improve cognition (eg, neurodevelopmental therapy [original format], handling, postural reactions and alignment). ^{34,35,39}	Children with or at high risk of CP (all motor types)
7	Communication	Conditional	For	Face-to-face nurturing with vocalizations, joint attention, and reciprocal-interaction interventions	We suggest parents engage their infant via face-to-face to talk, singing, using baby talk, and showing emotion when communicating, ⁴⁰⁻⁴² since infants have a clear preference for faces and share affect states with caregivers. We suggest learning to read the infant's microexpressions and eye pointing when motor impairment precludes nonverbal gestures ^{41,43} ; face-to-face interactions with the parent or caregiver's face as the visual target for infants with a visual impairment ^{41,44} ; assessment of parental mental health for its effect on communication ⁴⁰ ; and watchful interpretation to understand whether the cause of impaired vocalization and gestural skills is motoric, communicative, cognitive, or all of these.	Preverbal infants with or at high risk of CP (all motor types)
8	Communication	Conditional	For	Transactional speech-language and communication interventions	We suggest teaching parents and caregivers to build relational connections and reciprocal communication exchanges to foster active communication. ^{45,46} We suggest parent-infant transaction programs and Hanen therapy for improvements in communication skills and expressive language acquisition ^{47,48} ; the Mother-Infant Transaction Program (from a neonatal intensive care unit stay to 90 d postdischarge) to foster parental understanding of infant state regulation, sleep-wake cycles, joint interaction, and engagement ^{47,49} ; PremieStart to recognize and minimize stress responses in infants born preterm ⁴⁷ ; and Hanen It Takes Two to Talk therapy (6-8 sessions) to foster parental understanding of responsivity to their child's attempts at communication in a positive, prompt, and intentional manner. ⁵⁰	Children with or at high risk of CP suspected to be nonverbal or with emerging verbal ability
9	Eating and drinking	Conditional	For	Softer food consistencies	We suggest softened food consistencies to enhance feeding safety and efficiency. ⁵¹⁻⁵⁵	Children with or at high risk of CP and dysphagia

(continued)

Table. Recommendations (continued)

No.	Domain	Strength	Direction	Intervention	Key recommendations	Target population
10	Eating and drinking	Conditional	(1) For and (2) against	Slightly reclined or upright positioning	(1) We suggest a slightly reclined or upright position to enhance feeding safety and efficiency ⁵¹⁻⁵³ and (2) we suggest against very reclined positions that may exacerbate swallowing deficits. ⁵³	Children with or at high risk of CP and dysphagia
Complication prevention						
11	Vision	Conditional	For	Correction of strabismus	We suggest surgical correction of strabismus coupled with esotropia and/or exotropia to achieve good alignment of the eyes and sensorial binocular fusion. ⁵⁶	Children with or at high risk of mild CP and strabismus, by 2 y of age
12	Vision	Conditional	For	Visual training	We suggest early visual training programs to improve visual functions and attention to visual stimuli. ⁵⁷	Children with or at high risk of CP and cerebral visual impairment
13	Vision	Conditional	For	Color contrast cues	We suggest early provision of high-contrast/color visual stimulation in an interactive and contingent manner to improve visual orientation and mobility ⁵⁸⁻⁶¹ and social and physical environment adaptations to accommodate vision, such as high-contrast stimuli and light directed at the visual target.	Children with or at high risk of CP and cerebral visual impairment
14	Sleep	Conditional	For	Sleep hygiene	We suggest implementing sleep hygiene, including structuring a bedtime routine in a dark and quiet environment, ⁶²⁻⁶⁶ positive routines, controlled crying and comforting, and gradual extinction or sleep remodeling, as well as written diaries to monitor sleep patterns. ⁶⁶	Children with or at high risk of CP (all motor types)
15	Sleep	Strong	Against	Stimulating activities before bedtime	We recommend against stimulating activities, such as watching television or other screens and vigorous play during the lead-in to bedtime; this is to avoid inadequate or poor sleep plus excessive daytime sleepiness. ^{62-65,67}	Children with CP (all motor types)
16	Sleep	Conditional	For	Melatonin	We suggest considering melatonin after discussing risks, benefits, and family preferences. ⁶⁸⁻⁷⁶ Note: melatonin has not been approved for adults, children, or infants by the US Food and Drug Administration.	Children with or at high risk of CP and poor sleep onset and/or cerebral visual impairment
17	Sleep	Conditional	For	Apnea management	We suggest conventional staged apnea management approaches (eg, continuous positive airway pressure, steroids, surgical management) and referral to a sleep specialist. ⁷⁷⁻⁷⁹	Children with or at high risk of CP and sleep apnea
18	Sleep	Conditional	For	Spasticity management to improve sleep	We suggest trialing baclofen and/or botulinum toxin to reduce spasms and pain in an effort to improve sleep behavior. ^{80,81}	Children with or at high risk of CP and sleep disturbance from spasticity
19	Sleep	Conditional	Against	Sleep positioning systems	We recommend against using sleep positioning systems; they elevate the risk for gastroesophageal reflux, breathing difficulties, and death from unintentional asphyxiation. ^{64,82,83}	Children with or at high risk of CP and sleep disturbance
20	Sleep	Conditional	Against	Complementary and alternative medicine	We recommend against osteopathy and acupuncture for improving sleep. ^{84,85} Benefits do not appear to outweigh harms (eg, anecdotal reports of serious adverse events and poor tolerance, including crying and elevating cortisol levels), and effective alternatives exist.	Children with or at high risk of CP and sleep disturbance
21	Tone	Conditional	For	Comprehensive hypertonia management	We suggest commencement of comprehensive, goal-directed hypertonia management for hypertonia causing pain or interfering with motor development. ^{86,87} Hypertonia management should be considered in conjunction with the selection of motor interventions. ⁸⁸	Children with or at high risk of CP and hypertonia
22	Musculoskeletal	Conditional	For	Regular use of standing equipment for positioning	We suggest regular use of standing equipment for positioning as part of an active intervention program, to potentially decrease hip migration percentage and maintain hip abduction range of motion. ⁸⁹⁻⁹¹	Children with or at high risk of CP and risk of hip dysplasia, at the age when weight-bearing in standing would begin in children who are non-weight bearing
23	Musculoskeletal	Conditional	For	Ankle-foot orthosis	We suggest ankle-foot orthoses should be worn to improve or maintain dorsiflexion range of motion. ⁹² Note: ankle-foot orthoses may restrict active movement (eg, pulling to stand) but provide stability in standing. The optimal timing for prescription is unknown.	Children with CP at risk of ankle contracture
Parent support						
24	Mental health	Conditional	For	Evidence-based mental health therapies for parents	We suggest targeted, evidence-based mental health interventions. ⁹³	Parents/caregivers experiencing stress, anxiety, depression, or trauma

(continued)

Table. Recommendations (continued)

No.	Domain	Strength	Direction	Intervention	Key recommendations	Target population
25	Mental health	Conditional	For	Cognitive behavioral therapy	We suggest psychological interventions grounded in cognitive behavioral therapy ^{93,94} to decrease parental depression and anxiety.	Parents/caregivers experiencing stress, anxiety, depression, or trauma
26	Parenting	Conditional	For	Supporting parents to carry out kangaroo care	We suggest kangaroo care to promote maternal psychological adjustment and strengthening the relational bond. ⁹⁵	All infants born preterm or at low birth weight with or at high risk of CP and their mothers
27	Parenting	Conditional	For	Musical therapy, including musical interactions	We suggest music therapy including musical interactions between parents and their infants to promote infant well-being and reduce maternal anxiety. ⁹⁶	Infants born preterm with or at high risk of CP and their parents
28	Parenting	Conditional	For	Attachment support and coaching	We suggest coaching parental sensitivity and mutually enjoyable parent-infant interactions (from birth onwards) to foster good parental mental health and well-being and strengthen relational bonds. ⁹⁴	All children with or at high risk of CP and their parents

Abbreviations: CIMT, constraint-induced movement therapy; CP, cerebral palsy.

General Best Practice Guiding Principles

Best practice principles should guide professional interactions and intervention provided to children for all 9 domains (Figure).

1. Children diagnosed with or at high risk of CP should be immediately referred for CP-specific and age-specific intervention.⁸
2. Goals should be set that are task-specific and context-specific, at the appropriate level of challenge, and updated regularly.^{25,100} Clinicians should provide coaching and education to increase knowledge and impart support for parents and caregivers.
3. Clinicians should support parents and caregivers to build parental capacity and expertise, prioritizing a positive parent-child relationship. Parents' goals and aspirations must be central to the intervention, with parent participation essential. Of particular importance is the need for frequent practice of the activities that lead to skilled movement and functional independence. Intervention environments and professional input are not sufficiently frequent to achieve the goals of early intervention programs.^{16,25,101}

Skills Development

Interventions to Improve Motor Skills (Recommendations 1-4),

Applicable to All Types of Cerebral Palsy

Two systematic reviews^{17,102} and 9 RCTs^{16,18-22,25,26,103} were identified. Child-initiated movement, targeted motor training activities, and task-specific and context-specific exercises have the potential to maximize functional outcomes.¹⁰⁰ Repetition and intensity of practice optimize outcomes. Coaching families to engage their child in playful but targeted training ensures an adequate dose of practice. Therapy approaches that rely on specific therapist handling techniques, such as passive simulation of normal movements, were not supported by the evidence. It is important to support families to prioritize their relationship with their child, embed practice into daily routines, and use environmental enrichment to stimulate learning.^{17,102}

Interventions to Improve Motor Skills (Recommendations 1-4),

Applicable to Unilateral Cerebral Palsy (Hemiplegia)

Constraint-induced movement therapy (CIMT) and bimanual therapy^{22,26} improve function of the upper limbs in children with unilateral CP, and both are effective in older children with CP at an equal dose.⁶ Based on recent studies in children with upper limb asym-

metry, both are recommended with clinical reasoning, including parental preferences to determine the best approach for each child.¹⁰⁴

Interventions to Improve Cognition (Recommendations 5-6),

Applicable to All Types of Cerebral Palsy

There were no CP-specific cognitive systematic reviews found for children younger than 2 years. Eleven RCTs^{16,19,23,29,33-35,39,105-108} measured effects of early intervention strategies. A Cochrane meta-analysis¹⁰⁹ on the effectiveness of early intervention for infants born preterm supported small sustained gains for cognition. Most studies excluded infants with brain injuries, limiting the application of results to CP.¹⁰⁹ Early technology is assumed important to advance cognition in infants with severe physical disability. One systematic review¹¹⁰ of the benefits of assistive technology in infants and young children (3 months to 8 years and 9 months) with a range of disabilities supported moderate to large effects on cognitive outcomes. Specific information on CP could not be extracted from this review.¹¹⁰

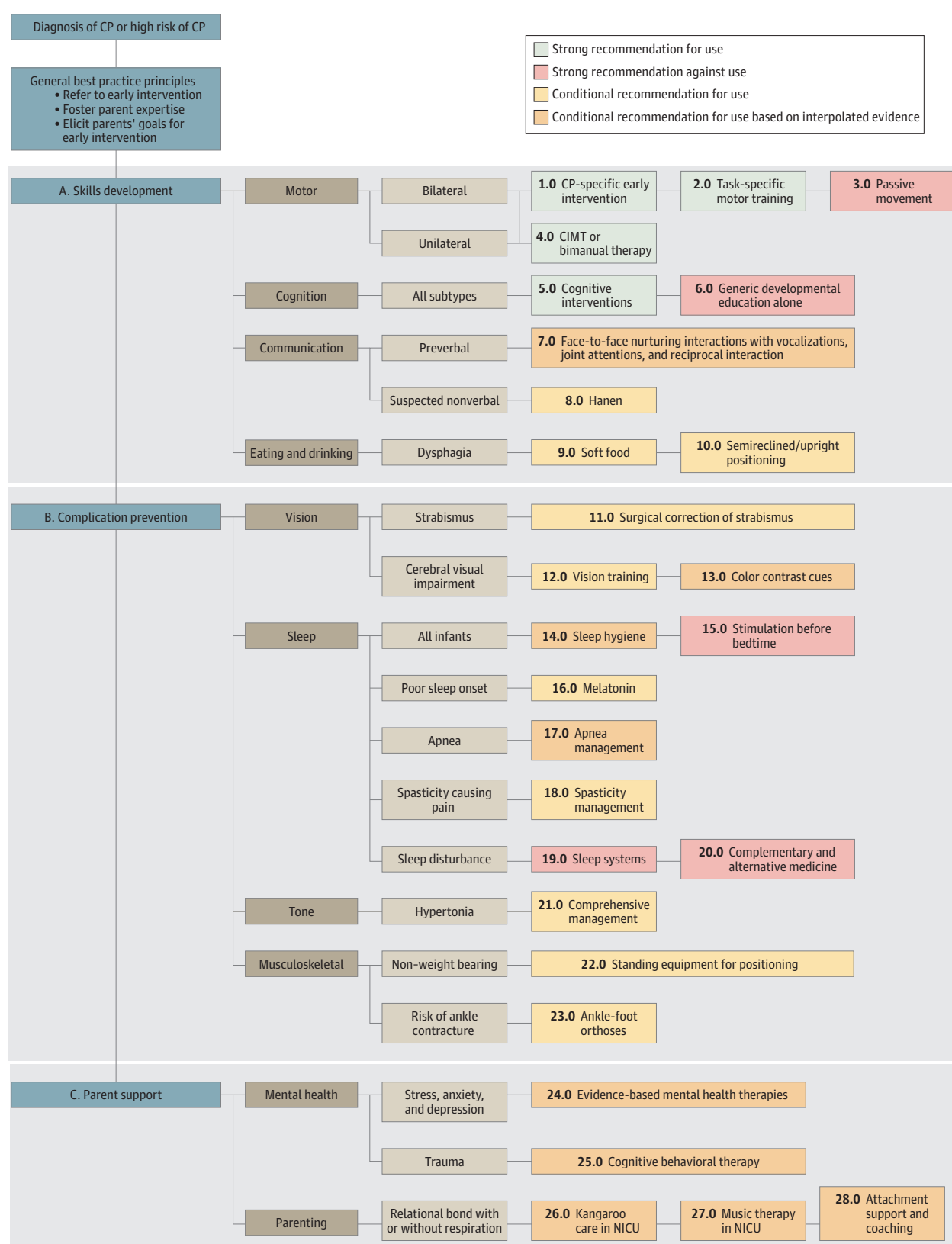
Environmental enrichment plus family engagement in task-specific and context-specific active learning that incorporates infant-generated motor and cognitive actions has a positive outcome.^{19,111} Tasks and toys may require adaptation or careful selection to accommodate the physical disability, without minimizing environmental and cognitive task demands. Relying on generic developmental education or assuming benefits to cognition resulting from motor intervention alone is insufficient.¹¹¹ There are no risks for providing age-appropriate and skill level-appropriate environmental enrichment and encouraging active learning. Parents want to be engaged in supporting their children's development but need support.¹¹² However, motor interventions with limited engagement of the child or that provide very general developmental education may not affect cognitive development in children with CP younger than 2 years.^{105,113}

Interventions to Promote Communication (Recommendations 7-8)

There were no CP-specific child speech and language interventions found. Two systematic reviews^{43,45} addressed communication for children at high risk, defined as those requiring neonatal intensive care or with other diagnoses who are at high risk for developmental delays. Recommendations do not apply to children with severe hearing loss.

Newborns are nonverbal but communicative. The acquisition of verbal speech and comprehension develops during early childhood.

Figure. General Best Practice Guiding Principles



CIMT indicates constraint-induced movement therapy; CP, cerebral palsy; NICU, neonatal intensive care unit.

Preverbal communication depends on the auditory processing of speech sounds and interpretation of social cues.^{40,114-116} Children who are developing typically perceive language as a social behavior and detect differences between languages and the emotional intent of communicators.¹¹⁷ One in 2 children with CP have difficulties engaging in reciprocal verbal speech,¹¹⁸⁻¹²⁰ and between 19% and 32% are nonverbal^{118,120,121} and may require augmentative and alternative communication.¹²² The 3 studies on augmentative and alternative communication¹¹⁰ identified were of insufficient quality to make strong recommendations. Clinicians need to comprehensively consider parents' preferences when offering this intervention.

Longitudinal studies assessing speech outcomes in toddlers with CP indicate that an inability to speak at 2 years is associated with poorer speech and language ability at 4 years.¹²³ For children with emerging verbal communication and those suspected of being nonverbal, the benefits of parent-child transactional programs (eg, Hanen) include improvements in communication skills and expressive language acquisition.^{43,45} Coaching assists parents or caregivers to create an effective environment for child communication. The intensity and group nature of some of the programs might limit feasibility.

Interventions to Promote Eating and Drinking (Recommendations 9-10), Applicable to Infants and Children With Dysphagia

There were 9 systematic reviews found.^{51-53,124-129} One review⁵² focused exclusively on children younger than 2 years, with others including broader age groups (eg, 16 months-3 years).

Evidence supports the use of softer food consistencies and upright supported positioning. No risks were reported for modifying food consistencies; however, different food consistencies have been associated with different levels of risk.^{54,55} Although improvements¹²⁴ in swallowing may be achieved through positioning modifications, reclined positions may exacerbate particular swallowing deficits.⁵³ Although interventions (ie, oral sensorimotor therapy, parent training, feeding devices, and modifications to positioning and food consistency) may provide benefits, further high-quality research is needed.

There is insufficient evidence regarding the benefits and harms of neuromuscular electrical stimulation, oral sensorimotor therapy, or surgical interventions (eg, gastrostomy) to inform recommendations. For children at considerable risk of aspiration, gastrostomy may be the only viable intervention to provide adequate nutrition.

Complication Prevention

Interventions to Improve Vision (Recommendations 11-13)

One in 10 children with CP have severe vision impairment or blindness⁷; up to 70% have some cerebral visual impairment.¹³⁰ Cerebral visual impairment is not often diagnosed in children younger than 2 years. One systematic review¹³¹ found only a few studies on vision interventions in infants and children with CP or at risk.

Applicable to Infants and Children With Mild CP and Strabismus | Children with CP may have strabismus.⁵⁶ Untreated strabismus causes a loss of depth perception, double vision, visual disorientation, and lower self-esteem.¹³² For children with amblyopia, occlusion therapy using an eye patch to cover the nonamblyopic eye is usual care.⁵⁶ Early surgical correction of esotropia and exotropia may be beneficial when performed to approximate surgery schedules for chil-

dren developing typically; surgeries completed by 2 years are optimal. Some experts recommend early surgery for mild CP, to gain better-quality fusion.

Applicable to Infants and Children With Confirmed or Suspected Cerebral Visual Impairment

| Early commencement of visual training is recommended to improve attention to visual stimuli and the use of available visual functions.⁵⁸ Within the context of parent-child interactions and goal-oriented play, the social and physical environment should be visually adapted to meet the child's needs.¹³³ High-contrast stimuli, light directed at the visual target, and multisensory experiences are recommended.^{57,59}

Interventions to Promote Sleep (Recommendations 14-20)

Applicable to All Types of Cerebral Palsy | No systematic reviews or RCTs were identified on sleep intervention for children younger than 2 years. Most of the published research on interventions was about other neurodevelopmental disorders.^{62-65,134,135}

Children with CP are 5 times more likely to have a sleep disorder than children developing typically.⁶²⁻⁶⁵ Sleep disturbances negatively affect quality of life for children and parents, with treatment having the potential to improve the well-being of the whole family.¹³⁴ Caregiver-provided interventions for children younger than 2 years were ranked as the most preferable interventions in a large survey of parents of children with CP. Untreated sleep disturbance can seriously affect academic performance and behavior.¹³⁶ Clinicians should identify the cause of the disturbance (eg, apnea, epilepsy, anxiety, pain, spasticity, cerebral visual impairment, reflux) and apply evidence-based interventions.^{63,65,135}

Treatment for sleep disorders should establish good sleep hygiene with parent-based education and behavioral interventions with parental preferences for sleep interventions.^{62,66,67,137-139} A structured, age-appropriate bedtime routine and a dark and quiet environment should be promoted. Maintaining regular bedtime and waking times may strengthen and train circadian mechanisms to promote rapid sleep onset. Potentially stimulating activities, such as watching television or other screens and vigorous play, should be avoided prior to bedtime.⁶²⁻⁶⁵ Educating parents about sleep and the treatable influences that promote or disrupt sleep is recommended, as is creating a quiet but enjoyable bedtime routine and moving gradually toward the child's sleep onset.^{137,138}

Controlled crying or modified extinction (ie, structured fading of parental/caregiver presence and physical contact to teach tolerance) is recommended to reduce crying and teach solo sleeping in infants developing typically. The approach is supported by multiple clinical trials and efficacious for fading resistance to bedtime and nighttime awakenings in toddlers.¹³⁹ Sleep experts have cautioned against using extinction behavioral techniques in infants younger than 6 months, because crying increases cortisol levels (potentially affecting brain development) and affects attachment.¹⁴⁰ These concerns are less prevalent for modified extinction protocols incorporating parent responsivity.¹⁴¹ These recommendations may be applicable, despite the lack of empirical research in the CP population, and have been conditionally recommended.

Applicable to Infants and Children With Poor Sleep Onset | Specific drugs, such as melatonin, are used for disturbed sleep in children

with neurological dysfunction, including those with visual impairment with poor day-night light differentiation.^{65,68-73} Melatonin can increase seizure activity in rare cases⁷⁴; however, recent studies have not confirmed this proconvulsive effect of melatonin, even in children with active epilepsy.^{75,142}

Applicable to Infants and Children With Sleep Apnea | Infants and children with CP can have sleep apnea, and the risks of harm from untreated apnea are serious.^{62,143} Conventional, staged apnea management approaches are recommended (eg, continuous positive airway pressure, steroids, and surgical management).^{77,78}

There is little research posthospital discharge on effective treatment of apnea in infants and children with or at high risk of cerebral palsy; nor is there consensus from systematic reviews on apnea management in children developing typically.^{78,79} Less invasive interventions are tried, first including continuous positive airway pressure and intranasal steroids, although infants and children often have poor tolerance to continuous positive airway pressure.^{78,79} Referral to a sleep specialist is recommended.

Applicable to Infants and Children With Sleep Disturbance Due to Spasticity | Infants with severe physical disability may experience severe sleep disturbance from involuntary movements, pain arising from muscle spasms, and/or hypertonia. Given the long-term detrimental effects of sleep disorders, baclofen and/or Botulinum toxin A should be considered to reduce spasms and pain to improve sleep.^{80,144}

Applicable to Infants and Children With Sleep Disturbance | For infants awoken by extraneous movements, nonpharmacological management, including safe swaddling, may help dampen these movements.⁸² Care should be taken to ensure the hips are not positioned in extension and adduction because of the risk of hip dysplasia.⁸³ Sleep positioning systems are not recommended⁶⁴ for infants, given the elevated risk for gastroesophageal reflux, breathing difficulties, and death.

Families may wish to trial complementary and alternative medicine treatments (such as osteopathy or massage), but the evidence is sparse and controversial for improving sleep.^{84,145-147} There are anecdotal reports of harm and low tolerance. Potential benefits vs harms need to be weighed (such as crying during treatment, procedural anxiety), and the treatments are not recommended because effective alternatives exist.

Interventions to Promote Reduction in Muscle Tone (Recommendation 21), Applicable to Infants and Children With Hypertonia

There was 1 systematic review found for the study population.⁸⁸ Management of tone in young children is not well described, with minimal high-quality evidence supporting pharmacological management for children younger than 2 years.

Hypertonicity is a major contributor to secondary impairments that progressively leads to activity and participation restrictions.¹⁴⁸ Secondary impairments include the development of contractures and deformities,¹⁴⁹ muscle stiffness, and abnormal motor control. Pharmacological management of hypertonia in children with CP is the standard of care in most high-income countries.

For hypertonia causing pain or interfering with motor development, management should be considered. Treatment planning

should consider the child's functional, personal, and environmental factors and be goal directed. There is limited evidence to suggest botulinum toxin is safe and effective for hypotonia management in children younger than 2 years when administered within a comprehensive treatment program. The outcome of botulinum toxin on developing muscle is unknown, and a conservative approach is recommended. A systematic review¹⁵⁰ identifying the rate of adverse events in children younger than 2 years was consistent with the existing literature for children older than 2 years, in whom adverse events are typically mild and localized.¹⁵¹ Management must be regularly monitored using standardized measurements of tone to inform decision-making.

Interventions to Prevent Musculoskeletal Impairments (Recommendations 22-23)

There were no systematic reviews or RCTs found for interventions to prevent musculoskeletal impairments for our population. There are 2 RCTs^{92,152} for older children with CP. There is high-quality evidence with promising results for increasing bone mineral density with a standing program.⁸⁹ Several studies included children younger than 5 years in addition to older children. Prevention of impairments should begin before age 2 years, and there is evidence of effective treatments for children older than 2 years.

Applicable to Infants and Children Who Are Non-Weight Bearing | The benefits of weight-bearing through standing is supported even in children younger than 5 years with CP. Standing equipment, including prone and supine standers and thermoplastic standing shells, are commonly used in infants and children requiring support. In older children with CP, regular standing in equipment is associated with improved bone density,¹⁵³ but this appears not to have been confirmed in those younger than 2 years. Standing support should be used when necessary to complement a treatment plan that primarily promotes action.

Applicable to Infants and Children With Risk of Ankle Contracture | Ankle-foot orthoses may be beneficial⁹² for maintaining range of motion and standing but may restrict active movement. There was insufficient evidence to recommend the timing of ankle-foot orthoses in infants and children with CP.

Parent Support

Mental Health and Parenting (Recommendations 24-28), Applicable to Parents Who Experience Stress, Anxiety, Depression, or Trauma No systematic reviews and 3 RCTs^{19,33,105} met inclusion criteria. Using broader age search terms and snowballing, a further 6 reviews^{93,94,96,154,155} were identified.

Parents of children with CP are at higher risk of mental health problems. Interventions targeting parent-infant interaction, psychosocial support, and psychoeducation may be helpful for strengthening parent-infant relationships and parental mental health.¹⁵⁴ For the infant in intensive care, skin-to-skin contact (kangaroo care)⁹⁵ and music therapy⁹⁶ can be helpful. Cognitive behavioral therapy has benefits for ameliorating parental depressive and anxious symptoms.^{93,94} Parenting interventions that incorporate acceptance and commitment therapy demonstrate improvements in maternal mental health for families of older children.¹⁵⁶

Discussion

We strongly recommend a comprehensive multidisciplinary approach. When an infant is diagnosed with or at high risk for CP, we recommend comprehensive screening for comorbidities. Feeding and sleep disorders may interfere with motor and cognitive skills because the infant is trying to learn in a suboptimal background of pain, low caloric fuel, and irritability. Anticipating secondary impairments enables timely access to interventions, which requires intentional communication among professionals.^{14,112} Evidence-based and empathic communication with parents is necessary as new issues and concerns are raised, empowering parents to seek help.¹⁵⁷ Supporting parents and their relationship with their child is fundamental to comprehensive early intervention; however, it is not always prioritized. Evidence from studies of parents of infants born preterm indicates probable benefits from interventions that focus on the supporting parenting role; however, we found little evidence that specifically addressed parent interventions after an early diagnosis.¹⁵⁸ Evidence-based mental health interventions are applicable to parents of infants and children newly diagnosed with CP.

There were no CP-specific RCTs found on improving sleep or communication. Low-level evidence for augmentative and alterna-

tive communication appears promising, but more rigorous studies are needed. Interventions to improve visual function and cognition are lacking, despite these co-impairments affecting quality of life.

The heterogeneity of motor severity compounded by varying comorbidities confound between-group differences in RCTs. Intervention trials may discover true effects when samples include participants with similar types, topographies, or severities. Challenges, such as small sample sizes, heterogeneity, and group designs that calculate mean results, are problematic. Advanced statistical techniques, such as bayesian modeling, pragmatic trials, and adaptive designs, might provide answers.

Limitations

There are limited studies from the target population. Many trials are currently underway, and recommendations may change. We excluded literature published in languages other than English.

Conclusions

Intervention should begin at diagnosis of CP or high risk of CP. Early targeted intervention builds on a critical developmental time for plasticity of developing systems. Intervention referrals for each domain should be specific to the recommendations.

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Author Affiliations: Cerebral Palsy Alliance Research Institute, Brain Mind Centre, Discipline of Child and Adolescent Health, The University of Sydney, Sydney, New South Wales, Australia (C. Morgan, Badawi, Karlsson, McIntyre, Thornton); University of Southern California, Los Angeles (Fetters, Dusing); Department of Clinical and Molecular Medicine, Norwegian University of Science and Technology, Trondheim, Norway (Adde); Clinic and Clinical Services, St Olavs Hospital, Trondheim University Hospital, Trondheim, Norway (Adde); Grace Centre for Newborn Care, Children's Hospital at Westmead, Westmead, New South Wales, Australia (Badawi, Loughran-Fowlds); IRCCS Fondazione Stella Maris, Pisa, Italy (Bancalè, Chorna, Cioni, Guzzetta); The University of Queensland, St Lucia, Queensland, Australia (Boyd, Mak, Whittingham); University of Pisa, Pisa, Italy (Cioni, Guzzetta); National Institutes of Health, Bethesda, Maryland (Damiano); Faculty of Rehabilitation Medicine, University of Alberta, Edmonton, Alberta, Canada (Darrah); University Medical Center Utrecht, Utrecht University, Utrecht, the Netherlands (de Vries); Division of Phoniatrics, Medical University of Graz, Austria (Einspieler); Karolinska Institutet, Stockholm, Sweden (Eliasson, Krumlinde-Sundholm); University of California, San Francisco, San Francisco (Ferriero); Holland Bloorview Kids Rehabilitation Hospital, Department of Paediatrics, University of Toronto, Toronto, Ontario, Canada (Fehlings); Department of Women's and Children's Health, Karolinska Institutet, Stockholm, Sweden (Forsberg); Teachers College, Columbia University, New York, New York (Gordon); The Royal Children's Hospital,

Melbourne, Australia (Greaves, A. Morgan); Department of Pediatrics, University of Groningen, University Medical Center Groningen, Groningen, the Netherlands (Hadders-Algra); Duquesne University, Pittsburgh, Pennsylvania (Harbourne); University Children's Hospital Zurich, Zurich, Switzerland (Latal); Nationwide Children's Hospital, The Ohio State University, Columbus (Maitre); Orygen, Parkville, Victoria, Australia (Mei); University of Melbourne, Parkville, Victoria, Australia (Mei, A. Morgan); Murdoch Children's Research Institute, Melbourne, Victoria, Australia (Mei, A. Morgan, Sanchez, Spittle); Makerere University, Kampala, Uganda (Kakooza-Mwesige); Pediatric Neurology Unit, Fondazione Policlinico Universitario A. Gemelli, Università Cattolica del Sacro Cuore, Rome, Italy (Romeo); Department of Physiotherapy, University of Melbourne, Parkville, Victoria, Australia (Spittle); The University of Sydney, Sydney, Australia (Shepherd, Novak); Perth Children's Hospital, Nedlands, Western Australia, Australia (Valentine); Curtin University, Perth, Australia (Ward); Eugene Child Development and Rehabilitation Center, Oregon Health and Science University, Eugene (Zamany).

Author Contributions: Drs C. Morgan and Fetters had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Concept and design: C. Morgan, Fetters, Adde, Badawi, Boyd, Cioni, de Vries, Dusing, Ferriero, Gordon, Greaves, Guzzetta, Loughran-Fowlds, Maitre, Romeo, Sanchez, Spittle, Shepherd, Valentine, Novak.

Acquisition, analysis, or interpretation of data: C. Morgan, Fetters, Adde, Bancalè, Boyd, Chorna, Damiano, Darrah, Dusing, Einspieler, Eliasson, Fehlings, Forsberg, Guzzetta, Hadders-Algra, Harbourne, Karlsson, Krumlinde-Sundholm, Latal, Mak, Maitre, McIntyre, Mei, A. Morgan, Kakooza-Mwesige, Sanchez, Spittle, Thornton,

Valentine, Ward, Whittingham, Zamany, Novak. Drafting of the manuscript: C. Morgan, Fetters, Boyd, Chorna, Dusing, Greaves, Harbourne, Krumlinde-Sundholm, Maitre, A. Morgan, Romeo, Sanchez, Spittle, Valentine, Ward, Whittingham, Zamany, Novak.

Critical revision of the manuscript for important intellectual content: C. Morgan, Fetters, Adde, Badawi, Bancalè, Boyd, Cioni, Damiano, Darrah, de Vries, Dusing, Einspieler, Eliasson, Ferriero, Fehlings, Forsberg, Gordon, Guzzetta, Hadders-Algra, Karlsson, Krumlinde-Sundholm, Latal, Loughran-Fowlds, Mak, Maitre, McIntyre, Mei, A. Morgan, Kakooza-Mwesige, Romeo, Sanchez, Spittle, Shepherd, Thornton, Valentine, Whittingham, Zamany, Novak.

Statistical analysis: Mak, Sanchez.

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REFERENCES

- Centers for Disease Control and Prevention. Cerebral Palsy. Published 2020. Accessed April 7, 2021. <https://www.cdc.gov/ncbddd/cp/index.html>
- Cerebral Palsy Alliance Research Institute. *Australian Cerebral Palsy Register Report*. Cerebral Palsy Alliance Research Institute; 2018.
- Gincota Buftac E, Andersen GL, Torstein V, Jahnsen R. Cerebral palsy in Moldova: subtypes, severity and associated impairments. *BMC Pediatr*. 2018;18(1):332. doi:10.1186/s12887-018-1305-6
- Khandaker G, Muhit M, Karim T, et al. Epidemiology of cerebral palsy in Bangladesh: a population-based surveillance study. *Dev Med Child Neurol*. 2019;61(5):601-609. doi:10.1111/dmcn.14013
- Kakooza-Mwesige A, Andrews C, Peterson S, Wabwire Mangu F, Eliasson AC, Forsberg H. Prevalence of cerebral palsy in Uganda: a population-based study. *Lancet Glob Health*. 2017;5(12):e1275-e1282. doi:10.1016/S2214-109X(17)30374-1
- Novak I, Morgan C, Fahey M, et al. State of the evidence traffic lights 2019: systematic review of interventions for preventing and treating children with cerebral palsy. *Curr Neurol Neurosci Rep*. 2020;20(2):3. doi:10.1007/s11910-020-1022-z
- Novak I, Hines M, Goldsmith S, Barclay R. Clinical prognostic messages from a systematic review on cerebral palsy. *Pediatrics*. 2012;130(5):e1285-e1312. doi:10.1542/peds.2012-0924
- Novak I, Morgan C, Adde L, et al. Early, accurate diagnosis and early intervention in cerebral palsy: advances in diagnosis and treatment. *JAMA Pediatr*. 2017;171(9):897-907. doi:10.1001/jamapediatrics.2017.1689
- Spittle AJ, Morgan C, Olsen JE, Novak I, Cheong JLY. Early diagnosis and treatment of cerebral palsy in children with a history of preterm birth. *Clin Perinatol*. 2018;45(3):409-420. doi:10.1016/j.clp.2018.05.011
- Brouwers MC, Kho ME, Browman GP, et al; AGREE Next Steps Consortium. AGREE II: advancing guideline development, reporting and evaluation in health care. *CMAJ*. 2010;182(18):E839-E842. doi:10.1503/cmaj.090449
- da Costa Santos CM, de Mattos Pimenta CA, Nobre MR. The PICO strategy for the research question construction and evidence search. *Rev Lat Am Enfermagem*. 2007;15(3):508-511. doi:10.1590/S0104-11692007000300023
- Burns PB, Rohrich RJ, Chung KC. The levels of evidence and their role in evidence-based medicine. *Plast Reconstr Surg*. 2011;128(1):305-310. doi:10.1097/PRS.0b013e318219c171
- Kolb B, Harker A, Gibb R. Principles of plasticity in the developing brain. *Dev Med Child Neurol*. 2017;59(12):1218-1223. doi:10.1111/dmcn.13546
- Byrne R, Noritz G, Maitre NL; NCH Early Developmental Group. Implementation of early diagnosis and intervention guidelines for cerebral palsy in a high-risk infant follow-up clinic. *Pediatr Neurol*. 2017;76:66-71. doi:10.1016/j.pediatrneurol.2017.08.002
- Guttmann K, Flibotte J, DeMauro SB. Parental perspectives on diagnosis and prognosis of neonatal intensive care unit graduates with cerebral palsy. *J Pediatr*. 2018;203:156-162. doi:10.1016/j.jpeds.2018.07.089
- Dusing SC, Harbourne RT, Lobo MA, et al. A physical therapy intervention to advance cognitive and motor skills: a single subject study of a young child with cerebral palsy. *Pediatr Phys Ther*. 2019;31(4):347-352. doi:10.1097/PEP.0000000000000635
- Morgan C, Darragh J, Gordon AM, et al. Effectiveness of motor interventions in infants with cerebral palsy: a systematic review. *Dev Med Child Neurol*. 2016;58(9):900-909. doi:10.1111/dmcn.13105
- Campbell SK, Cole W, Boynewicz K, et al. Behavior during tethered kicking in infants with periventricular brain injury. *Pediatr Phys Ther*. 2015;27(4):403-412. doi:10.1097/PEP.0000000000000173
- Morgan C, Novak I, Dale RC, Guzzetta A, Badawi N. Single blind randomised controlled trial of GAME (Goals-Activity-Motor Enrichment) in infants at high risk of cerebral palsy. *Res Dev Disabil*. 2016;55:256-267. doi:10.1016/j.ridd.2016.04.005
- Kolobe THA, Fagg AH. Robot reinforcement and error-based movement learning in infants with and without cerebral palsy. *Phys Ther*. 2019;99(6):677-688. doi:10.1093/ptj/pzz043
- Holmström L, Eliasson AC, Almeida R, et al. Efficacy of the small step program in a randomized controlled trial for infants under 12 months old at risk of cerebral palsy (CP) and other neurological disorders. *J Clin Med*. 2019;8(7):E1016. doi:10.3390/jcm8071016
- Eliasson AC, Nordstrand L, Ek L, et al. The effectiveness of Baby-CIMT in infants younger than 12 months with clinical signs of unilateral-cerebral palsy: an explorative study with randomized design. *Res Dev Disabil*. 2018;72:191-201. doi:10.1016/j.ridd.2017.11.006
- Hielkema T, Blauw-Hospers CH, Dirks T, Drijver-Messelink M, Bos AF, Hadders-Algra M. Does physiotherapeutic intervention affect motor outcome in high-risk infants? an approach combining a randomized controlled trial and process evaluation. *Dev Med Child Neurol*. 2011;53(3):e8-e15. doi:10.1111/j.1469-8749.2010.03876.x
- Akhbari Ziegler S, Dirks T, Hadders-Algra M. Coaching in early physical therapy intervention: the COPCA program as an example of translation of theory into practice. *Disabil Rehabil*. 2019;41(15):1846-1854. doi:10.1080/09638288.2018.1448468
- Morgan C, Novak I, Dale RC, Badawi N. Optimising motor learning in infants at high risk of cerebral palsy: a pilot study. *BMC Pediatr*. 2015;15(30):30. doi:10.1186/s12887-015-0347-2
- Chamudot R, Parush S, Rigbi A, Horovitz R, Gross-Tsur V. Effectiveness of modified constraint-induced movement therapy compared with bimanual therapy home programs for infants with hemiplegia: a randomized controlled trial. *Am J Occup Ther*. 2018;72(6):p1, p9. doi:10.5014/ajot.2018.025981
- Will B, Galani R, Kelche C, Rosenzweig MR. Recovery from brain injury in animals: relative efficacy of environmental enrichment, physical exercise or formal training (1990-2002). *Prog Neurobiol*. 2004;72(3):167-182. doi:10.1016/j.pneurobio.2004.03.001
- Nithianantharajah J, Hannan AJ. Enriched environments, experience-dependent plasticity and disorders of the nervous system. *Nat Rev Neurosci*. 2006;7(9):697-709. doi:10.1038/nrn1970
- Blauw-Hospers CH, Dirks T, Hulshof LJ, Bos AF, Hadders-Algra M. Pediatric physical therapy in infancy: from nightmare to dream? a two-arm randomized trial. *Phys Ther*. 2011;91(9):1323-1338. doi:10.2522/ptj.20100205
- Zanon MA, Pacheco RL, Latorraca COC, Martimbianco ALC, Pachito DV, Riera R. Neurodevelopmental treatment (Bobath) for children with cerebral palsy: a systematic review. *J Child Neurol*. 2019;34(11):679-686. doi:10.1177/0883073819852237
- Chamudot R, Parush S, Rigbi A, Horovitz R, Gross-Tsur V. Effectiveness of modified constraint-induced movement therapy compared with bimanual therapy home programs for infants with hemiplegia: a randomized controlled trial. *Am J Occup Ther*. 2018;72(6):p1, p9. doi:10.5014/ajot.2018.025981
- Eliasson AC, Sjöstrand L, Ek L, Krumlinde-Sundholm L, Tedroff K. Efficacy of baby-CIMT: study protocol for a randomised controlled trial on infants below age 12 months, with clinical signs of unilateral CP. *BMC Pediatr*. 2014;14:141. doi:10.1186/1471-2431-14-141
- Ohgi S, Fukuda M, Akiyama T, Gima H. Effect of an early intervention programme on low birthweight infants with cerebral injuries. *J Paediatr Child Health*. 2004;40(12):689-695. doi:10.1111/j.1440-1754.2004.00512.x
- Palmer FB, Shapiro BK, Allen MC, et al. Infant stimulation curriculum for infants with cerebral palsy: effects on infant temperament, parent-infant interaction, and home environment. *Pediatrics*. 1990;85(3 Pt 2):411-415.
- Palmer FB, Shapiro BK, Wachtel RC, et al. The effects of physical therapy on cerebral palsy: a controlled trial in infants with spastic diplegia. *N Engl J Med*. 1988;318(13):803-808. doi:10.1056/NEJM19880313181302
- Mahoney G, Kaiser A, Girolametto L, et al. Parent education in early intervention: a call for a renewed focus. *Topics in Early Childhood Special Education*. 1999;19(3):131-140. doi:10.1177/02711249901900301
- Nores M, Barnett WS. Benefits of early childhood interventions across the world: (under) investing in the very young. *Economics of Education Review*. 2010;29(2):271-282. doi:10.1016/j.econedurev.2009.09.001
- Protzko J, Aronson J, Blair C. How to make a young child smarter: evidence from the database of

- raising intelligence. *Perspect Psychol Sci*. 2013;8(1):25-40. doi:10.1177/1745691612462585
40. Reddihough DS, King J, Coleman G, Catanese T. Efficacy of programmes based on conductive education for young children with cerebral palsy. *Dev Med Child Neurol*. 1998;40(11):763-770. doi:10.1111/j.1469-8749.1998.tb12345.x
41. Matthews D. *Pragmatic Development in First Language Acquisition*. John Benjamins Publishing Co; 2014. doi:10.1075/tilar.10
42. Meltzoff AN, Moore MK. Imitation in newborn infants: exploring the range of gestures imitated and the underlying mechanisms. *Dev Psychol*. 1989;25(6):954-962. doi:10.1037/0012-1649.25.6.954
43. Soderstrom M, Morgan JL. Twenty-two-month-olds discriminate fluent from disfluent adult-directed speech. *Dev Sci*. 2007;10(5):641-653. doi:10.1111/j.1467-7687.2006.00605.x
44. Pennington L, Akor WA, Laws K, Goldbart J. Parent-mediated communication interventions for improving the communication skills of preschool children with non-progressive motor disorders. *Cochrane Database Syst Rev*. 2018;7(7):CD012507. doi:10.1002/14651858.CD012507.pub2
45. Pereira SA, Pereira Junior A, Costa MF, et al. A comparison between preterm and full-term infants' preference for faces. *J Pediatr (Rio J)*. 2017;93(1):35-39. doi:10.1016/j.jpeds.2016.04.009
46. Chorna O, Hamm E, Cummings C, Fetters A, Maitre NL. Speech and language interventions for infants aged 0 to 2 years at high risk for cerebral palsy: a systematic review. *Dev Med Child Neurol*. 2017;59(4):355-360. doi:10.1111/dmcn.13342
47. Pennington L, Akor WA, Laws K, Goldbart J. Parent-mediated communication interventions for improving the communication skills of preschool children with non-progressive motor disorders. *Cochrane Database Syst Rev*. 2018;7(7):CD012507. doi:10.1002/14651858.CD012507.pub2
48. Milgrom J, Newnham C, Martin PR, et al. Early communication in preterm infants following intervention in the NICU. *Early Hum Dev*. 2013;89(9):755-762. doi:10.1016/j.earlhumdev.2013.06.001
49. Newnham CA, Milgrom J, Skouteris H. Effectiveness of a modified Mother-Infant Transaction Program on outcomes for preterm infants from 3 to 24 months of age. *Infant Behav Dev*. 2009;32(1):17-26. doi:10.1016/j.infbeh.2008.09.004
50. Kynø NM, Ravn IH, Lindemann R, Fagerland MW, Smeby NA, Torgersen AM. Effect of an early intervention programme on development of moderate and late preterm infants at 36 months: a randomized controlled study. *Infant Behav Dev*. 2012;35(4):916-926. doi:10.1016/j.infbeh.2012.09.004
51. Pennington L, Thomson K, James P, Martin L, McNally R. Effects of it takes two to talk—the Hanen program for parents of preschool children with cerebral palsy: findings from an exploratory study. *J Speech Lang Hear Res*. 2009;52(5):1121-1138. doi:10.1044/1092-4388(2009)07-0187
52. Ferluga ED, Archer KR, Sathe NA, et al; Agency for Healthcare Research and Quality. Interventions for feeding and nutrition in cerebral palsy: comparative effectiveness review No. 94, AHRQ publication No. 13-EHC015-EF. Published 2013. Accessed April 9, 2021. <https://www.ncbi.nlm.nih.gov/books/NBK132442/>
53. Khamis A, Novak I, Morgan C, et al. Motor learning feeding interventions for infants at risk of cerebral palsy: a systematic review. *Dysphagia*. 2020;35(1):1-17. doi:10.1007/s00455-019-10016-x
54. Snider L, Majnemer A, Darsaklis V. Feeding interventions for children with cerebral palsy: a review of the evidence. *Phys Occup Ther Pediatr*. 2011;31(1):58-77. doi:10.3109/01942638.2010.523397
55. Weir K, McMahon S, Barry L, Ware R, Masters IB, Chang AB. Oropharyngeal aspiration and pneumonia in children. *Pediatr Pulmonol*. 2007;42(11):1024-1031. doi:10.1002/ppul.20687
56. Beal J, Silverman B, Bellant J, Young TE, Klontz K. Late onset necrotizing enterocolitis in infants following use of a xanthan gum-containing thickening agent. *J Pediatr*. 2012;161(2):354-356. doi:10.1016/j.jpeds.2012.03.054
57. Ghasia F, Brunstrom-Hernandez J, Tychsens L. Repair of strabismus and binocular fusion in children with cerebral palsy: gross motor function classification scale. *Invest Ophthalmol Vis Sci*. 2011;52(10):7664-7671. doi:10.1167/iov.10-6906
58. Lanners J, Piccioni A, Fea F, Goergen E. Early intervention for children with cerebral visual impairment: preliminary results. *J Intellect Disabil Res*. 1999;43(Pt 1):1-12. doi:10.1046/j.1365-2788.1999.43120106.x
59. Alimović S, Katušić A, Mejaški-Bošnjak V. Visual stimulations' critical period in infants with perinatal brain damage. *NeuroRehabilitation*. 2013;33(2):251-255. doi:10.3233/NRE-130952
60. Malkowicz DE, Myers G, Leisman G. Rehabilitation of cortical visual impairment in children. *Int J Neurosci*. 2006;116(9):1015-1033. doi:10.1080/00207450600553505
61. Sonksen PM, Petrie A, Drew KJ. Promotion of visual development of severely visually impaired babies: evaluation of a developmentally based programme. *Dev Med Child Neurol*. 1991;33(4):320-335. doi:10.1111/j.1469-8749.1991.tb14883.x
62. Sonksen PM, Wade AM, Proffitt R, Heavens S, Salt AT. The Sonksen logMAR test of visual acuity: II, age norms from 2 years 9 months to 8 years. *J AAPOS*. 2008;12(1):18-22. doi:10.1016/j.jaaapos.2007.04.019
63. Angriman M, Caravale B, Novelli L, Ferri R, Bruni O. Sleep in children with neurodevelopmental disabilities. *Neuropediatrics*. 2015;46(3):199-210. doi:10.1055/s-0035-1550151
64. Simard-Tremblay E, Constantin E, Gruber R, Brouillette RT, Shevell M. Sleep in children with cerebral palsy: a review. *J Child Neurol*. 2011;26(10):1303-1310. doi:10.1177/0883073811408902
65. Galland BC, Elder DE, Taylor BJ. Interventions with a sleep outcome for children with cerebral palsy or a post-traumatic brain injury: a systematic review. *Sleep Med Rev*. 2012;16(6):561-573. doi:10.1016/j.smrv.2012.01.007
66. Mercuri E RD. Cerebral Palsy. In Accardo J. *Sleep in Children With Neurodevelopmental Disabilities: an Evidence-Based Guide*. Springer;2019. doi:10.1007/978-3-319-98414-8_13
67. Halal CSE, Nunes ML. Education in children's sleep hygiene: which approaches are effective? a systematic review. *J Pediatr (Rio J)*. 2014;90(5):449-456. doi:10.1016/j.jpeds.2014.05.001
68. Carter B, Rees P, Hale L, Bhattacharjee D, Paradar MS. Association between portable screen-based media device access or use and sleep outcomes: a systematic review and meta-analysis. *JAMA Pediatr*. 2016;170(12):1202-1208. doi:10.1001/jamapediatrics.2016.2341
69. Wasdell MB, Jan JE, Bomben MM, et al. A randomized, placebo-controlled trial of controlled release melatonin treatment of delayed sleep phase syndrome and impaired sleep maintenance in children with neurodevelopmental disabilities. *J Pineal Res*. 2008;44(1):57-64.
70. Dodge NN, Wilson GA. Melatonin for treatment of sleep disorders in children with developmental disabilities. *J Child Neurol*. 2001;16(8):581-584. doi:10.1177/088307380101600808
71. Ross C, Davies P, Whitehouse W. Melatonin treatment for sleep disorders in children with neurodevelopmental disorders: an observational study. *Dev Med Child Neurol*. 2002;44(5):339-344. doi:10.1111/j.1469-8749.2002.tb00821.x
72. Appleton RE, Jones AP, Gamble C, et al. The use of melatonin in children with neurodevelopmental disorders and impaired sleep: a randomised, double-blind, placebo-controlled, parallel study (MENDS). *Health Technol Assess*. 2012;16(40):i-239. doi:10.3310/hta16400
73. Schwichtenberg AJ, Malow BA. Melatonin treatment in children with developmental disabilities. *Sleep Med Clin*. 2015;10(2):181-187. doi:10.1016/j.jsmc.2015.02.008
74. Lin-Dyken DC, Dyken ME. Use of melatonin in young children for sleep disorders. *Infants and Young Children*. 2002;15(1):20. doi:10.1097/00001163-200210000-00005
75. Sheldon SH. Pro-convulsant effects of oral melatonin in neurologically disabled children. *Lancet*. 1998;351(9111):1254. doi:10.1016/S0140-6736(05)79321-1
76. Gringras P, Gamble C, Jones AP, et al; MENDS Study Group. Melatonin for sleep problems in children with neurodevelopmental disorders: randomised double masked placebo controlled trial. *BMJ*. 2012;345(7882):e6664. doi:10.1136/bmj.e6664
77. Romeo DM. Use of melatonin for sleep disorders in children with cerebral palsy. *Brain Disorders & Therapy*. 2015;4(5). doi:10.4172/2168-975X.1000201
78. Nørgaard M, Stagstrup C, Lund S, Poulsen A. To bubble or not? a systematic review of bubble continuous positive airway pressure in children in low- and middle-income countries. *Journal of Tropical Pediatrics*. 2020;66(3):339-353. doi:10.1093/tropej/fmz069
79. Kuhle S, Urschitz MS, Eitner S, Poets CF. Interventions for obstructive sleep apnea in children: a systematic review. *Sleep Med Rev*. 2009;13(2):123-131. doi:10.1016/j.smrv.2008.07.006
80. Manickam PV, Shott SR, Boss EF, et al. Systematic review of site of obstruction identification and non-CPAP treatment options for children with persistent pediatric obstructive sleep apnea. *Laryngoscope*. 2016;126(2):491-500. doi:10.1002/lary.25459
81. Binay Safer V, Ozbudak Demir S, Ozkan E, Demircioglu Guner F. Effects of botulinum toxin serotype A on sleep problems in children with cerebral palsy and on mothers sleep quality and depression. *Neurosciences (Riyadh)*. 2016;21(4):331-337. doi:10.17712/nsj.2016.4.20160207
82. Ramstad K, Jahnsen R, Lofterod B, Skjeldal OH. Continuous intrathecal baclofen therapy in children with cerebral palsy—when does improvement

- emerge? *Acta Paediatr.* 2010;99(11):1661-1665. doi:10.1111/j.1651-2227.2009.01596.x
83. Ohgi S, Akiyama T, Arisawa K, Shigemori K. Randomised controlled trial of swaddling versus massage in the management of excessive crying in infants with cerebral injuries. *Arch Dis Child.* 2004;89(3):212-216. doi:10.1136/adc.2002.025064
84. Clarke NMP. Swaddling and hip dysplasia: an orthopaedic perspective. *Arch Dis Child.* 2014;99(1):5-6. doi:10.1136/archdischild-2013-304143
85. Wyatt K, Edwards V, Franck L, et al. Cranial osteopathy for children with cerebral palsy: a randomised controlled trial. *Arch Dis Child.* 2011;96(6):505-512. doi:10.1136/adc.2010.199877
86. Beider S, Moyer CA. Randomized controlled trials of pediatric massage: a review. *Evid Based Complement Alternat Med.* 2007;4(1):23-34. doi:10.1093/ecam/nel068
87. Tedroff K, Löwing K, Haglund-Akerlind Y, Gutierrez-Farewik E, Forsberg H. Botulinum toxin A treatment in toddlers with cerebral palsy. *Acta Paediatr.* 2010;99(8):1156-1162. doi:10.1111/j.1651-2227.2010.01767.x
88. Pascual-Pascual SI, Pascual-Castroviejo I. Safety of botulinum toxin type A in children younger than 2 years. *Eur J Paediatr Neurol.* 2009;13(6):511-515. doi:10.1016/j.ejpn.2008.10.006
89. Ward R, Reynolds JE, Bear N, Elliott C, Valentine J. What is the evidence for managing tone in young children with, or at risk of developing, cerebral palsy: a systematic review. *Disabil Rehabil.* 2017;39(7):619-630. doi:10.3109/09638288.2016.1153162
90. Macias-Merlo L, Bagur-Calafat C, Girabent-Farrés M, Stuber WA. Standing programs to promote hip flexibility in children with spastic diplegic cerebral palsy. *Pediatr Phys Ther.* 2015;27(3):243-249. doi:10.1097/PEP.0000000000000150
91. Martinsson C, Himmelmann K. Effect of weight-bearing in abduction and extension on hip stability in children with cerebral palsy. *Pediatr Phys Ther.* 2011;23(2):150-157. doi:10.1097/PEP.0b013e318218efc3
92. Pountney TE, Mandy A, Green E, Gard PR. Hip subluxation and dislocation in cerebral palsy—a prospective study on the effectiveness of postural management programmes. *Physiother Res Int.* 2009;14(2):116-127. doi:10.1002/pri.434
93. Zhao X, Xiao N, Li H, Du S. Day vs. day-night use of ankle-foot orthoses in young children with spastic diplegia: a randomized controlled study. *Am J Phys Med Rehabil.* 2013;92(10):905-911. doi:10.1097/PHM.0b013e318296e3e8
94. Kraljevic M, Warnock FF. Early educational and behavioral RCT interventions to reduce maternal symptoms of psychological trauma following preterm birth: a systematic review. *J Perinat Neonatal Nurs.* 2013;27(4):311-327. doi:10.1097/JPN.0b013e3182a8bfe2
95. Brecht C, Shaw RJ, Horwitz SM, John NH. Effectiveness of therapeutic behavioral interventions for parents of low birth weight premature infants: a review. *Infant Ment Health J.* 2012;33(6):651-665. doi:10.1002/imhj.21349
96. Athanasopoulou E, Fox JRE. Effects of kangaroo mother care on maternal mood and interaction patterns between parents and their preterm, low birth weight infants: a systematic review. *Infant Ment Health J.* 2014;35(3):245-262. doi:10.1002/imhj.21444
97. Bieleninik E, Ghetti C, Gold C. Music therapy for preterm infants and their parents: a meta-analysis. *Pediatrics.* 2016;138(3):e20160971. doi:10.1542/peds.2016-0971
98. Shea BJ, Hamel C, Wells GA, et al. AMSTAR is a reliable and valid measurement tool to assess the methodological quality of systematic reviews. *J Clin Epidemiol.* 2009;62(10):1013-1020. doi:10.1016/j.jclinepi.2008.10.009
99. Higgins JP, Altman DG, Gøtzsche PC, et al; Cochrane Bias Methods Group; Cochrane Statistical Methods Group. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *BMJ.* 2011;343:d5928. doi:10.1136/bmj.d5928
100. Andrews J, Guyatt G, Oxman AD, et al. GRADE guidelines: 14. going from evidence to recommendations: the significance and presentation of recommendations. *J Clin Epidemiol.* 2013;66(7):719-725. doi:10.1016/j.jclinepi.2012.03.013
101. Shepherd RB. The changing face of intervention in infants with cerebral palsy. In: Shepherd RB, ed. *Cerebral Palsy in Infancy.* Churchill Livingstone; 2014. doi:10.1016/B978-0-7020-5099-2.00001-7
102. Hielkema T, Hamer EG, Boxum AG, et al. LEARN2MOVE 0-2 years, a randomized early intervention trial for infants at very high risk of cerebral palsy: neuromotor, cognitive, and behavioral outcome. *Disabil Rehabil.* 2020;42(26):3752-3761. doi:10.1080/09638288.2019.1610508
103. Hadders-Algra M, Boxum AG, Hielkema T, Hamer EG. Effect of early intervention in infants at very high risk of cerebral palsy: a systematic review. *Dev Med Child Neurol.* 2017;59(3):246-258. doi:10.1111/dmcn.13331
104. van Balen LC, Dijkstra LJ, Dirks T, Bos AF, Hadders-Algra M. Early intervention and postural adjustments during reaching in infants at risk of cerebral palsy. *Pediatr Phys Ther.* 2019;31(2):175-183. doi:10.1097/PEP.0000000000000585
105. Maitre NL, Jeanvoine A, Yoder PJ, et al; BBOP group. Kinematic and somatosensory gains in infants with cerebral palsy after a multi-component upper-extremity intervention: a randomized controlled trial. *Brain Topogr.* 2020;33(6):751-766. doi:10.1007/s10548-020-00790-5
106. Badr LK, Garg M, Kamath M. Intervention for infants with brain injury: results of a randomized controlled study. *Infant Behav Dev.* 2006;29(1):80-90. doi:10.1016/j.infbeh.2005.08.003
107. Mayo NE. The effect of physical therapy for children with motor delay and cerebral palsy. A randomized clinical trial. *Am J Phys Med Rehabil.* 1991;70(5):258-267. doi:10.1097/0002060-199110000-00006
108. Nelson MN, White-Traut RC, Vasani U, et al. One-year outcome of auditory-tactile-visual-vestibular intervention in the neonatal intensive care unit: effects of severe prematurity and central nervous system injury. *J Child Neurol.* 2001;16(7):493-498. doi:10.1177/088307380101600706
109. Weindling AM, Hallam P, Gregg J, Klenka H, Rosenbloom L, Hutton JL. A randomized controlled trial of early physiotherapy for high-risk infants. *Acta Paediatr.* 1996;85(9):1107-1111. doi:10.1111/j.1651-2227.1996.tb14226.x
110. Spittle A, Orton J, Anderson PJ, Boyd R, Doyle LW. Early developmental intervention programmes provided post hospital discharge to prevent motor and cognitive impairment in preterm infants. *Cochrane Database Syst Rev.* 2015;(11):CD005495. doi:10.1002/14651858.CD005495.pub4
111. Dunst CJ, Trivette CM, Hamby DW, Simkus A. Systematic review of studies promoting the use of assistive technology devices by young children with disabilities. *Practical Evaluation Reports.* 2013;5(1).
112. Harbourne RT, Berger SE. Embodied cognition in practice: exploring effects of a motor-based problem-solving intervention. *Phys Ther.* 2019;99(6):786-796. doi:10.1093/ptj/pzz031
113. Byrne R, Duncan A, Pickar T, et al. Comparing parent and provider priorities in discussions of early detection and intervention for infants with and at risk of cerebral palsy. *Child Care Health Dev.* 2019;45(6):799-807. doi:10.1111/cch.12707
114. Hielkema T, Hadders-Algra M. Motor and cognitive outcome after specific early lesions of the brain—a systematic review. *Dev Med Child Neurol.* 2016;58(suppl 4):46-52. doi:10.1111/dmnc.13047
115. Reissland N, Kisilevsky BS, eds. *Fetal Development.* Springer; 2016. doi:10.1007/978-3-319-22023-9
116. Canfield CF, Saudino KJ. The influence of infant characteristics and attention to social cues on early vocabulary. *J Exp Child Psychol.* 2016;150:112-129. doi:10.1016/j.jecp.2016.05.005
117. P. Key A. Human Auditory Processing: Insights from cortical event-related potentials. *AIMS Neuroscience.* 2016;3(2):141-162. doi:10.3934/Neuroscience.2016.2.141
118. Liberman Z, Woodward AL, Kinzler KD. Preverbal infants infer third-party social relationships based on language. *Cogn Sci.* 2017;41(5)(suppl 3):622-634. doi:10.1111/cogs.12403
119. Zhang JY, Oskoui M, Shevell M. A population-based study of communication impairment in cerebral palsy. *J Child Neurol.* 2015;30(3):277-284. doi:10.1177/0883073814538497
120. Coleman A, Weir K, Ware RS, Boyd R. Predicting functional communication ability in children with cerebral palsy at school entry. *Dev Med Child Neurol.* 2015;57(3):279-285. doi:10.1111/dmnc.12631
121. Nordberg A, Miniscalco C, Lohmander A, Himmelmann K. Speech problems affect more than one in two children with cerebral palsy: Swedish population-based study. *Acta Paediatr.* 2013;102(2):161-166. doi:10.1111/apa.12076
122. Australian Cerebral Palsy Register. *Report of the Australian Cerebral Palsy Register, Birth Years 1993–2003.* Cerebral Palsy Alliance Research Institute; 2009.
123. Branson D, Demchak M. The use of augmentative and alternative communication methods with infants and toddlers with disabilities: a research review. *Augment Altern Commun.* 2009;25(4):274-286. doi:10.3109/07434610903384529
124. Hustad KC, Allison KM, Sakash A, McFadd E, Broman AT, Rathouz PJ. Longitudinal development of communication in children with cerebral palsy between 24 and 53 months: Predicting speech outcomes. *Dev Neurorehabil.* 2017;20(6):323-330. doi:10.1080/17518423.2016.1239135
125. Samson-Fang L, Butler C, O'Donnell M; AACPD. Effects of gastrostomy feeding in children with cerebral palsy: an AACPD evidence

- report. *Dev Med Child Neurol*. 2003;45(6):415-426. doi:10.1111/j.1469-8749.2003.tb00421.x
- 126.** Wilcox DD, Potvin M-C, Prelock PA. Oral motor interventions and cerebral palsy: using evidence to inform practice. *Early Intervention & School Special Interest Section Quarterly*. 2009;16(4):1-4.
- 127.** Ferluga ED, Sathe NA, Krishnaswami S, Mcpheeters ML. Surgical intervention for feeding and nutrition difficulties in cerebral palsy: a systematic review. *Dev Med Child Neurol*. 2014;56(1):31-43. <https://onlinelibrary.wiley.com/doi/10.1111/dmnc.12170>
- 128.** Gantasala S, Sullivan PB, Thomas AG. Gastrostomy feeding versus oral feeding alone for children with cerebral palsy. *Cochrane Database Syst Rev*. 2013;(7):CD003943. doi:10.1002/14651858.CD003943.pub3
- 129.** Morgan Angela T, Dodrill P, Ward Elizabeth C. Interventions for oropharyngeal dysphagia in children with neurological impairment. *Cochrane Database of Systematic Reviews*. 2012(10). doi:10.1002/14651858.CD009456.pub2
- 130.** Sleight G, Brocklehurst P. Gastrostomy feeding in cerebral palsy: a systematic review. *Arch Dis Child*. 2004;89(6):534-539.
- 131.** Ego A, Lidzba K, Brovedani P, et al. Visual-perceptual impairment in children with cerebral palsy: a systematic review. *Dev Med Child Neurol*. 2015;57(suppl 2):46-51. doi:10.1111/dmnc.12687
- 132.** Chorna OD, Guzzetta A, Maitre NL. Vision assessments and interventions for infants 0-2 years at high risk for cerebral palsy: a systematic review. *Pediatr Neurol*. 2017;76:3-13. doi:10.1016/j.pediatrneurol.2017.07.011
- 133.** Hatt Sarah R, Gnanaraj L. Interventions for intermittent exotropia. *Cochrane Database of Systematic Reviews*. 2013(5). doi:10.1002/14651858.CD003737.pub3.
- 134.** Sonksen PM, Petrie A, Drew KJ. Promotion of visual development of severely visually impaired babies: evaluation of a developmentally based programme. *Dev Med Child Neurol*. 1991;33(4):320-335. doi:10.1111/j.1469-8749.1991.tb14883.x
- 135.** Sandella DE, O'Brien LM, Shank LK, Warschausky SA. Sleep and quality of life in children with cerebral palsy. *Sleep Med*. 2011;12(3):252-256. doi:10.1016/j.sleep.2010.07.019
- 136.** Blackmer AB, Feinstein JA. Management of sleep disorders in children with neurodevelopmental disorders: a review. *Pharmacotherapy*. 2016;36(1):84-98. doi:10.1002/phar.1686
- 137.** Tanner K, Noritz G, Ayala L, et al. Assessments and interventions for sleep disorders in infants with or at high risk for cerebral palsy: a systematic review. *Pediatr Neurol*. 2020;50:887-894(20) 30348-9. doi:10.1016/j.pediatrneurol.2020.10.015
- 138.** Hoban TF. Sleep disorders in children. *Ann N Y Acad Sci*. 2010;1184(1):1-14. doi:10.1111/j.1749-6632.2009.05112.x
- 139.** Grigg-Damberger M, Ralls F. Treatment strategies for complex behavioral insomnia in children with neurodevelopmental disorders. *Curr Opin Pulm Med*. 2013;19(6):616-625. doi:10.1097/MCP.0b013e328365ab89
- 140.** Mindell JA, Kuhn B, Lewin DS, Meltzer LJ, Sadeh A; American Academy of Sleep Medicine. Behavioral treatment of bedtime problems and night wakings in infants and young children. *Sleep*. 2006;29(10):1263-1276.
- 141.** Blunden SL, Thompson KR, Dawson D. Behavioural sleep treatments and night time crying in infants: challenging the status quo. *Sleep Med Rev*. 2011;15(5):327-334. doi:10.1016/j.smrv.2010.11.002
- 142.** Blunden S, Dawson D. Behavioural sleep interventions in infants: plan B—combining models of responsiveness to increase parental choice. *J Paediatr Child Health*. 2020;56(5):675-679. doi:10.1111/jpc.14818
- 143.** Besag FMC, Vasey MJ, Lao KSJ, Wong ICK. Adverse events associated with melatonin for the treatment of primary or secondary sleep disorders: a systematic review. *CNS Drugs*. 2019;33(12):1167-1186. doi:10.1007/s40263-019-00680-w
- 144.** Shintani T, Asakura K, Ishi K, Yoshida M, Kataura A, Ogasawara H. [Obstructive sleep apnea in children with cerebral palsy]. *Nihon Jibiinkoka Gakkai Kaiho*. 1998;101(3):266-271. doi:10.3950/jibiinkoka.101.266
- 145.** Ramstad K, Jahnsen R, Lofterod B, Skjeldal OH. Continuous intrathecal baclofen therapy in children with cerebral palsy—when does improvement emerge? *Acta Paediatr*. 2010;99(11):1661-1665. doi:10.1111/j.1651-2227.2009.01596.x
- 146.** Duncan B, Barton L, Edmonds D, Blashill BM. Parental perceptions of the therapeutic effect from osteopathic manipulation or acupuncture in children with spastic cerebral palsy. *Clin Pediatr (Phila)*. 2004;43(4):349-353. doi:10.1177/000992280404300406
- 147.** Glew GMFM, Hagland S, Bjornson K, Beider S, McLaughlin JF. Survey of the use of massage for children with cerebral palsy. *Int J Ther Massage Bodywork*. 2010;3(4):10-15.
- 148.** Beider S, Moyer CA. Randomized controlled trials of pediatric massage: a review. *Evid Based Complement Alternat Med*. 2007;4(1):23-34. doi:10.1093/ecam/nel068
- 149.** Ramstad K, Jahnsen R, Skjeldal OH, Diseth TH. Parent-reported participation in children with cerebral palsy: the contribution of recurrent musculoskeletal pain and child mental health problems. *Dev Med Child Neurol*. 2012;54(9):829-835. doi:10.1111/j.1469-8749.2012.04341.x
- 150.** Mathewson MA, Chambers HG, Girard PJ, Tenenhaus M, Schwartz AK, Lieber RL. Stiff muscle fibers in calf muscles of patients with cerebral palsy lead to high passive muscle stiffness. *J Orthop Res*. 2014;32(12):1667-1674. doi:10.1002/jor.22719
- 151.** Bourseul JS, Molina A, Lintanf M, et al. Early botulinum toxin injections in infants with musculoskeletal disorders: a systematic review of safety and effectiveness. *Arch Phys Med Rehabil*. 2018;99(6):1160-1176.e5. doi:10.1016/j.apmr.2017.11.013
- 152.** Paget SP, Swinney CM, Burton KLO, Bau K, O'Flaherty SJ. Systemic adverse events after botulinum neurotoxin A injections in children with cerebral palsy. *Dev Med Child Neurol*. 2018;60(11):1172-1177. doi:10.1111/dmnc.13995
- 153.** Law MC, Darrah J, Pollock N, et al. Focus on function: a cluster, randomized controlled trial comparing child- versus context-focused intervention for young children with cerebral palsy. *Dev Med Child Neurol*. 2011;53(7):621-629. doi:10.1111/j.1469-8749.2011.03962.x
- 154.** Hough JP, Boyd RN, Keating JL. Systematic review of interventions for low bone mineral density in children with cerebral palsy. *Pediatrics*. 2010;125(3):e670-e678. doi:10.1542/peds.2009-0292
- 155.** Benzies KM, Magill-Evans JE, Hayden KA, Ballantyne M. Key components of early intervention programs for preterm infants and their parents: a systematic review and meta-analysis. *BMC Pregnancy Childbirth*. 2013;13(suppl 1):S10. doi:10.1186/1471-2393-13-S1-S10
- 156.** Athanaspoulou E, Fox JR. Effects of kangaroo mother care on maternal mood and interaction patterns between parents and their preterm, low birth weight infants: a systematic review. *Infant Ment Health J*. 2014;35(3):245-262. doi:10.1002/imhj.21444
- 157.** Whittingham K, Sanders MR, McKinlay L, Boyd RN. Parenting intervention combined with acceptance and commitment therapy: a trial with families of children with cerebral palsy. *J Pediatr Psychol*. 2016;41(5):531-542. doi:10.1093/jpepsy/jsv118
- 158.** Novak I, Morgan C, McNamara L, Te Velde A. Best practice guidelines for communicating to parents the diagnosis of disability. *Early Hum Dev*. 2019;139:104841-104841. doi:10.1016/j.earlhumdev.2019.104841
- 159.** Reid A, Imrie H, Brouwer E, et al. "If I knew then what I know now": parents' reflections on raising a child with cerebral palsy. *Phys Occup Ther Pediatr*. 2011;31(2):169-183. doi:10.3109/O1942638.2010.540311