A systematic review of interventions for children with cerebral palsy: state of the evidence

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vention options. From an ICF perspective, CP impacts on a personÕs ÔfunctioningÕ, (inclusive of body structures [e.g. limbs], body functions [e.g. intellectual function], activities [e.g. walking], and participation [e.g. playing sport]), which in turn may cause ÔdisabilitiesÕ, such as impairments, activity limitations, and participation restrictions. Moreover, each person with CP lives within a personalized environment and thus their context also contributes to determining their independence, comprising personal factors (e.g. motivation) and environmental factors (e.g. architectural accessibility).[9,10] Thus, there are many potential problems a child with CP may face and seek intervention for. The Þeld has chosen a philosophical shift away from almost exclusively redressing physical impairments underlying functional problems to adopting an additional focus on maximizing childrenÕs environment, their independence in daily activities, and their community participation.[11] Furthermore, clinicians applying the recommended goal-based approach seek to choose interventions guided by what would best help the family achieve their goals.[12–14] Couple these philosophical preferences with widespread barriers to research implementation (such as limited time, insufÞcient library access, limited research appraisal skills, attitudinal blocks to research, and differing patient preferences), and there is no assurance that children with CP will receive evidence-based interventions.[1,15,16]

The aim of this paper was to describe systematically the best available evidence for CP interventions using the GRADE [17] system and to complement these Þndings with the Evidence Alert TrafÞc Light System[18] in order to provide knowledge translation guidance to clinicians about what to do. The purpose of rating the whole CP intervention evidence base within the one paper was to provide clinicians, managers, and policy-makers with a ÔhelicopterÕ view of best available intervention evidence that could be used to (1) inform decision-making by succinctly describing current evidence about CP interventions across the wide span of disciplines involved in care; (2) rapidly aid comparative clinical decision-making about similar interventions; and (3) provide a comprehensive resource that could be used by knowledge brokers to help prioritize the creation of knowledge translation tools to promote evidence implementation.[19]

METHOD

Study design

A systematic review of systematic reviews (i.e. the highest level of CP intervention research evidence available) was conducted in order to provide an overview of the current state of CP intervention evidence. Systematic reviews were preferentially sought since reviews provide a summary of large bodies of evidence and reviews help to explain differences among studies. Moreover, reviews limit bias which assists clinicians, managers, and policy-makers with decision-making about current best available evidence.[20] However, for interventions for which no systematic reviews existed, lower levels of evidence were included to illuminate the current state of the evidence.

Search strategy

Our review was carried out using a protocol based upon recommendations from the Cochrane Collaboration and PRISMA statements.[21,22] Relevant articles were identiÞed by searching the CINAHL (1983–2012); Cochrane Database of Systematic Reviews (1992–2013; www.cochrane.org); Database of Reviews of Effectiveness (DARE); EMBASE (1980–2012); ERIC; Google Scholar; MEDLINE (1956–2012); OTSeeker (www.otseeker.com); Physiotherapy Evidence Database (PEDro [www.pedro.fhs.usyd.edu.au]); Psychological database for Brain Impairment Treatment EfÞcacy (PsycBITE [www.psycbite.com]); PsycINFO (1935–2012); PubMED; and Speech Pathology Database for Best Interventions and Treatment EfÞcacy (speechBITE [www.speechbite.com]). Searches were supplemented by hand searching. The search of published studies was performed in July and August 2011 and updated in December 2012. Interventions and keywords for investigation were identiÞed using (1) contributing authorsÕ knowledge of the Þeld; (2) internationally recognized CP websites such as the American Academy of Cerebral Palsy and Developmental Medicine (www.aacpdm.org), *CanChild* (www.canchild.ca), the Cerebral Palsy Alliance (www.cerebralpalsy.org.au), Cincinnati ChildrenÕs Hospital (www.cincinnatichildrens.org), Karolinksa Insitutet (www.ki.se), NetChild (www.netchild.nl), NeuroDevNet (www.neurodevnet.ca), and Reaching for the Stars (www.reachingforthestars.org); and (3) the top 20 hits in Google using the search term Ôcerebral palsyÕ as an indicator of popular subject matter.

Electronic databases were searched with EBSCO host software using PICOs [patient/problemyAlli-

Evidence of Oxford levels 2 to 4 were included only if (1) level 1 evidence did not exist on the topic and then the next best available highest level of evidence was included; or if (2) level 2 randomized controlled trial(s) had been published since the latest systematic review, which substantially changed knowledge about the topic.

Second, retrieved bodies of evidence were coded using

Table I: I l s t s, s t v l l v l v ls, gr s t ff l g ts

	Intervention	Intervention outcome (ICF level)	Citations	Panel comments	Oxford evidence level	GRADE: Quality of evidence	GRADE: Strength of recommendation	Traf Þc light action
1	Acupuncture: electro-stimulation to scalp and body via needles and manual pressure	Improved gross motor function (A)	Zhang[25]	Insuf Þcient evidence	1	Low	Weak +	Yellow MEASURE
2	Alcohol: muscular injections to induce chemical denervation for treating local spasticity	Reduce muscle spasticity locally via injections (BS)	Delgado[26]	Insuf Þcient evidence to support, but BoNT-A exists as a highly effective alternative – therefore probably do not use alcohol unless BoNT-A total dose limitations in play	1	N/A	Weak –	Yellow MEASURE
3	Alternative and augmentative communication: technology alternatives to verbal speech, e.g. communication boards, speech generating devices	Improved general communication skills (A)	Pennington[27]	Lower-quality supporting evidence	1	Very low	Weak +	Yellow | MEASURE
		Improved communication skills of pre-school children (A)	Branson[28]	Lower-quality supporting evidence	1	Very low	Weak +	Yellow MEASURE
		Improved communication skills of conversational partners (P)	Pennington[29]	Lower-quality supporting evidence	1	Very low	Weak +	Yellow MEASURE
		Enhanced supplementation of verbal speech (A)	Hanson[30] Millar[31]	Lower-quality supporting evidence	1 1	Very low	Weak +	Yellow MEASURE
4	Animal-assisted therapy: service animals to provide companionship and assist with independence, e.g. seizure Þrst aid, door opening, crossing roads	Improved socialization and mood; reduced stress, anxiety and loneliness; and improved leisure (BS and P)	Mu ñoz Lasa[32]	Lower-quality supporting evidence	1	Very low	Weak +	Yellow MEASURE
		Improved independence via service dogs (P)	Winkle[33]	Lower-quality supporting evidence	1	Very low	Weak +	Yellow MEASURE
5	Anticonvulsants: medications to prevent seizures	Improved seizure control (BS)	–					

Table I: t

	Intervention	Intervention outcome (ICF level)	Citations	Panel comments	Oxford evidence level	GRADE		Traffic light action
						Quality of evidence	Strength of recommendation	
8	Behaviour therapy: positive behaviour support, behavioural interventions, and positive parenting	Improved child behaviour (from u.Toones						

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	Intervention	Intervention outcome (ICF level)	Citations	Panel comments	Oxford evidence level	GRADE: Quality of evidence	GRADE: Strength of recommendation	Traffic light action
38	Intrathecal baclofen (ITB): antispasticity medication delivered directly to the spinal cord via a pump surgically implanted within the abdomen	Reduced lower limb spasticity (BS)	Butler [130] Creedon [131] Dan [132] Delgado [26] Kolaski [133]	Predominantly low-quality supporting evidence. The size of the gains varies between studies	1 1 1 1 1	Low	Weak +	Yellow MEASURE
		Reduced upper limb spasticity (BS)	Butler [130] Creedon [131] Dan [132] Delgado [26] Kolaski [133]	Insufficient evidence. The effect on upper limb is less than for the lower limb and some authors question whether ITB is clinically worthwhile for the purposes of reducing upper limb spasticity	1 1 1 1 1	Low	Weak –	Yellow MEASURE
		Reduced dystonia (BS)	Albanese [134] Butler [130]	Lower-quality supporting evidence	1 1	Very low	Weak +	Yellow MEASURE
		Improved function and health related quality of life (A, P and PF)	Hoving [135] Hoving [136] Kolaski [133]	Lower-quality supporting evidence	2 2 1	Low	Weak +	Yellow MEASURE
		Improved walking ability in ambulant children (A)	Pin [137]	Insufficient evidence. Some children with CP improve but many experience adverse events including inability to walk	1	Very low	Weak –	Yellow MEASURE
39	Massage: therapeutic stroking and circular motions applied by a massage therapist to muscles to relieve pain and tension	Reduced pain (BS)	Hernandez-Reif [138] Nilsson [139]	Conflicting evidence	2 2	Low	Weak +	Yellow MEASURE
		Reduced spasticity (BS)	Alizad [140] Hernandez-Reif [138]	Conflicting evidence	2 2	Low	Weak +	Yellow MEASURE
		Improved function (A)	Hernandez-Reif [138]	Conflicting evidence	2	Low	Weak +	Yellow MEASURE
40	Neurodevelopmental therapy (NDT, Bobath): direct, passive handling and guidance to optimise function	Normalized movement (BS)	Brown [141] Butler [142]	Ineffective. No gains superior to other treatments	1 1	Low	Strong –	Red STOP
		Prevent contracture development (BS)	Brown [141] Butler [142]	Ineffective because immediate gains in range of motion observed within the session do not carry over	1 1	Low	Strong –	Red STOP
		Improved function (A)	Brown [141] Butler [142] Martin [143]	Conflicting systematic review evidence. Early reviews suggested no benefits. The more recent review included one new trial suggesting possible benefit of higher doses of NDT compared with lower doses of NDT; however, this is not a conventional method for establishing treatment efficacy and should be interpreted with caution. Other evidence shows that motor learning produces superior functional gains to NDT	1 1 1	Low	Weak –	Yellow MEASURE
		Enhanced social emotional and cognitive skills (BS and PF)	Brown [141] Butler [142]	Ineffective. No evidence to support claim	1 1	Low	Strong –	Red STOP
41	Occupational therapy after BoNT: improved hand use via CIMT, goal-directed training, strength training and functional hand splints. improved symptom management via casting and immobilisation splints	Improved goal achievement of upper limb activities (A)	Boyd [59] Fehlings [65] Hoare [70] Hoare [71] Lannin [99]	Effective	1 1 1 1 1	High	Strong +	Green GO

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	Intervention	Intervention outcome (ICF level)	Citations	Panel comments	Oxford evidence level	GRADE: Quality of evidence	GRADE: Strength of recommendation	Traffic light action
57	Strength training (resistance): use of progressively more challenging resistance to muscular contraction to build muscle strength and anaerobic endurance	Improved lower limb strength via progressive resistance training (BS)	Dodd [165] Effgen [78] Jeglinsky [166] Martin [143] Mockford [167] Scianni [168] Taylor [169]	Effective short term for improving muscle strength. Improved muscle strength does not carry over to function, other treatment approaches will be needed for functional gains	1 1 1 1 1 1 1	Low	Weak +	Yellow MEASURE
		Improved upper limb strength via progressive resistance training (BS)	Kim [170]	Effective short term for improving muscle strength	2	Low	Weak +	Yellow MEASURE
		Improved function via progressive resistance training (A)	Scianni [168]	Insufficient evidence	1	Low	Weak –	Yellow MEASURE
		Improved function via functional training using resistance within functional tasks (A)	Martin [143]	Lower-quality supporting evidence	1	Low	Weak +	Yellow MEASURE
58	Stretching: use of an external passive force (e.g. parent) exerted upon the limb to move it into a new and lengthened position	Contracture prevention via manual stretching (BS)	Katalinic [79] Wiart [171]	Ineffective. Comprehensive and robust meta-analysis showed no immediate, or short – to medium-term benefits (<7mo), but, since only a small number of CP studies were included within the review, it is not possible to be certain about this recommendation for CP	1 1	Moderate	Weak –	Yellow MEASURE
		Contracture prevention via splinting or positioning (BS)	Autti-Ramo [76] Pin [45] Teplicky [81]	Insufficient evidence	1 1 1	Low	Weak +	Yellow MEASURE
59	Therasuits: a breathable soft dynamic orthotic full body suit, designed to improve proprioception, reduce reflexes, restore synergies and provide resistance	Improved gross motor function (A)	Alagesan [172] Bailes [173]	Conflicting evidence. One trial suggests positive effect the other suggest no benefits	2 2	Low	Weak –	Yellow MEASURE
60	Tizanidine: antispasticity medication	Reduce spasticity (generalized) (BS)	Delgado [26]	Insufficient evidence	1	Low	Weak +	Yellow MEASURE
61	Treadmill training: walking practice on a treadmill, which includes partial body support	Improved weight bearing (BS)	Zwicker [174]	Lower-quality supporting evidence	1	Low	Weak +	Yellow MEASURE
		Improved functional walking (A)	Damiano [175] Mutlu [176] Willoughby [177] Zwicker [174]	Lower-level supporting evidence. However, overground walking more effective than partial body weight-supported treadmill training	1 1 1 1	Low	Weak +	Yellow MEASURE
62	Vitamin D (with our without calcium or growth hormones): dietary vitamin supplement for bone density	Improved bone mineral density (BS)	Fehlings [55] Hough [56]	Insufficient evidence	1 1	Low	Weak +	Yellow MEASURE
63	Vojta: therapist applied pressure to defined zones on the body whilst positioned in prone, supine or side lying, where the stimulus leads to automatically and involuntarily complex movement	Improve strength and movement, plus lessen severity of CP (BS)	Brandt [178] dÕAvignon [179] Kanda [180] Liu [181] Wu [182] Zhang [183] Zhao [188]	Conflicting evidence. Studies claim to ÔcureÕ early CP, which is not consistent with any of the other literature about CP having no known cure. Also the studies reported high dropout rates due to child distress. Studies have a high probability of bias, e.g. lack of: random sequence generation; concealed allocation, study blinding, psychometrically sound instruments; plus incomplete outcome data collection and selective reporting	2 2 3 2 2 2 2	Very low	Weak –	Yellow MEASURE

using the Oxford Levels of Evidence; a categorization using GRADE; a colour coding scheme using the Evidence

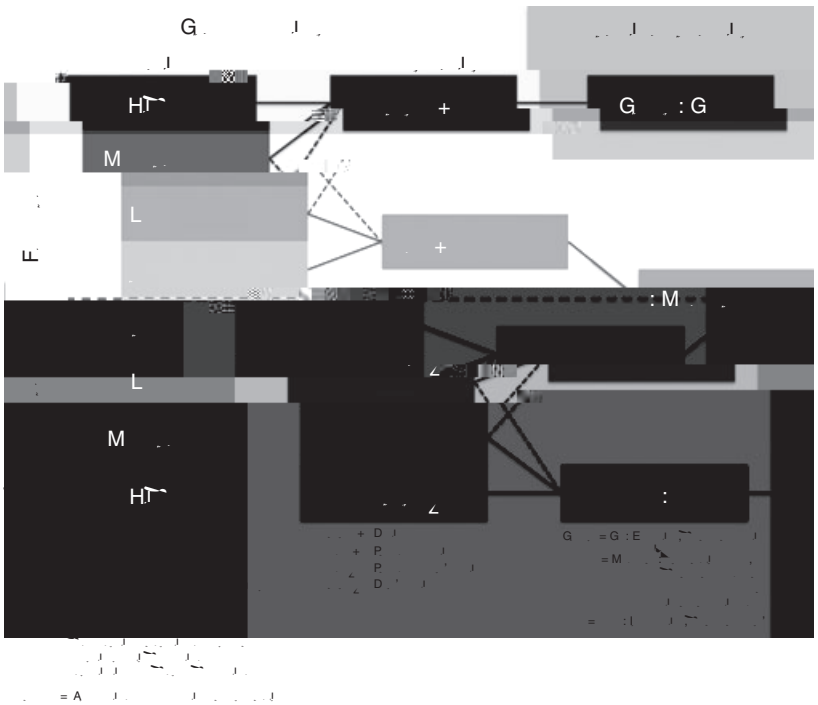


Figure 1: l t s t t G r ff g t yst .

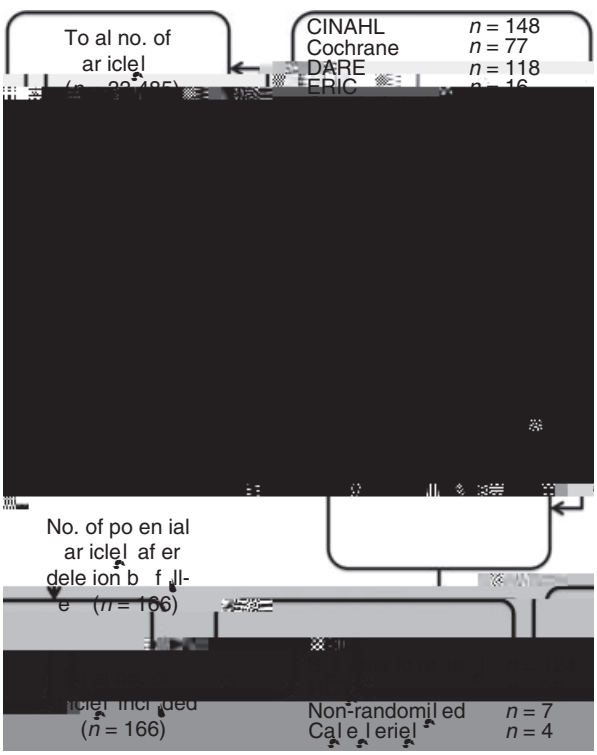


Figure 2: l gr f l rtl s.

166 included studies, the breakdown by level of evidence as rated on the Oxford Levels of Evidence was level 1 (*n*=124), 74%; level 2 (*n*=30), 18%; level 3 (*n*=6), 4%; and level 4 (*n*=6), 4%.

When the included articles were tallied in 5-year intervals by publication date, it was clear that the number of systematic reviews published about CP intervention had exponentially increased in recent years (Fig. 3).

Almost none (2 of 166) of the systematic reviews retrieved graded the body of evidence summarized using the GRADE system. We therefore carried out assignment of GRADEs using the recommended expert panel methodology. Using the GRADE system, of the 64 different CP interventions reviewed across 131 intervention outcomes 16% of outcomes assessed (*n*=21) were graded Ôdo itÕ (i.e. green light, go interventions); 58% (*n*=76) were graded Ôprobably do itÕ (i.e. yellow light, measure outcomes); 20% (*n*=26) were graded Ôprobably do not do itÕ (i.e. yellow light, measure outcomes; see Fig. 1); and 6% (*n*=8) were graded Ôdo not do itÕ (i.e. red light, stop interventions; see Fig. 1). In line with the appraisal criteria for this review, occupational therapy, physiotherapy, and medicine were the disciplines that encompassed the highest number of proven effective interventions for CP within their evidence base, which is not surprising given the long historical research emphasis on redressing the physical aspects of CP. In the Þelds of psychology, speech pathology, social work, and education, the evidence base for all interventions reviewed was lower level or inconclusive (yellow), but, in keeping with interdisciplinary care, psychologists and social

workers applied high-level evidence from other diagnostic groups (e.g. bimanual, cognitive behaviour therapy, counselling, Triple P[49]). In the Þeld of speech pathology, it is worth noting that it is difÞcult to conduct studies of augmentative and alternative communication (AAC) using conventional rigorous methodologies because included participants often have different disability types and, accordingly, differing levels of expressive, receptive, and social communication abilities. AAC interventions require multifactorial measurement because effective device utilization relies on changes in all of these domains from best-practice speech, language, and teaching strategies and from changing the mode of communication. Thus, adequately measuring and attributing interventions effects to each component of these integrated treatment approaches remains challenging. Amongst the alternative and complementary medicine interventions offered by some clinicians, the Þndings were of even poorer quality, because an even greater proportion of the interventions were proven ineffective. However, the real rate of ineffective alternative and complementary interventions may be even higher as so many had to be excluded from this review as a result of the lack of any published peer-reviewed literature about the approaches (e.g. advanced biomechanical rehabilitation).

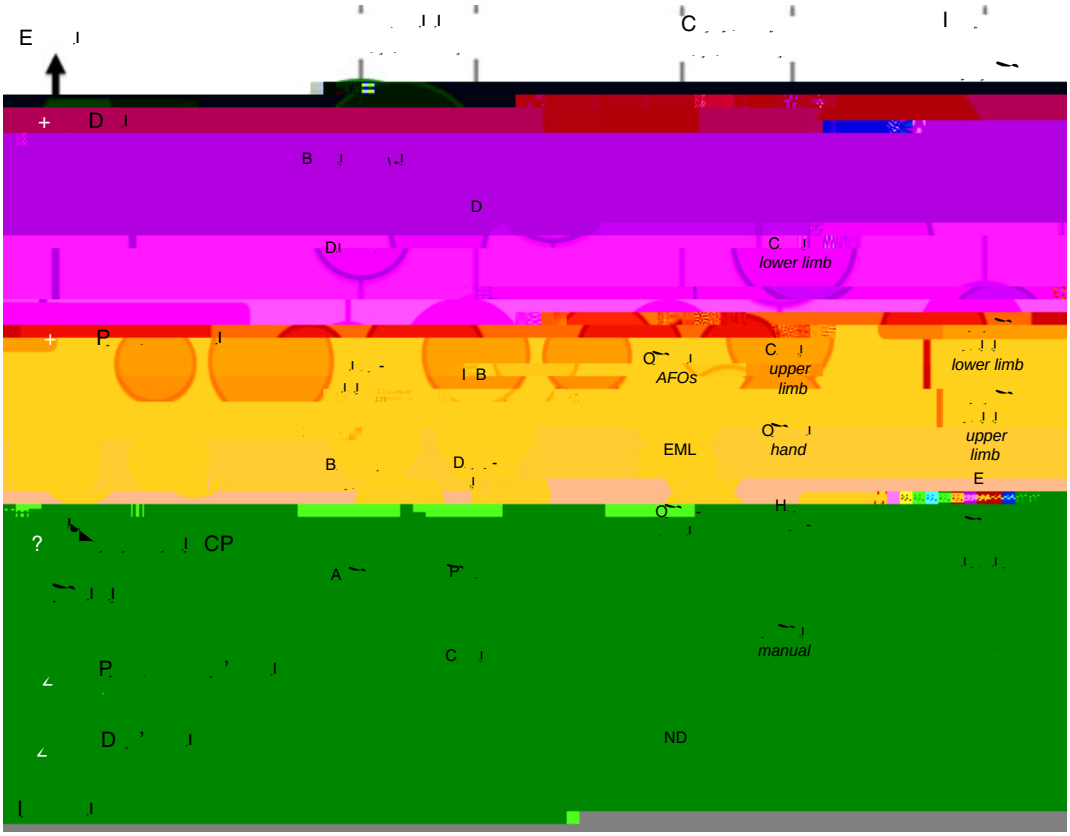
Each intervention was coded using the ICF by the interventionÕs desired outcome. Out of the 131 intervention outcomes for children with CP identiÞed in this study, n=66 (51%) were aimed at the body structures and function level; n=39 (30%) were aimed at the activity level; n=7 (5%) were aimed at the participation level; n=8 (6%) were aimed at the environment level; and the remaining n=11 (8%) were aimed at combinations of ICF levels.

Green light go interventions

In the papers retrieved, the following CP interventions were shown to be effective: (1) botulinum toxin (BoNT), diazepam, and selective dorsal rhizotomy for reducing muscle spasticity; (2) casting for improving and maintaining ankle range of motion; (3) hip surveillance for maintaining hip joint integrity; (4) constraint-induced movement therapy, bimanual training, context-focused therapy, goal-directed/functional training, occupational therapy following BoNT, and home programmes for improving motor activity performance and/or self-care; (5) Þtness training for improving Þtness; (6) bisphosphonates for improving bone density; (7) pressure care for reducing the risk of pressure ulcers; and (8) anticonvulsants for managing seizures (despite no CP-speciÞc anticonvulsant evidence existing, the panel rated the strength of the recommendation as strong plus (do it) because good-quality evidence supports anticonvulsants in non-CP populations,[191] and serious harm, even death, can arise from no treatment).

Green light effective interventions were mapped against the ICF by the outcomes that had been measured in the literature and the corresponding trafÞc light code was applied (Table II). First, Table II shows that green-light effective interventions were all aimed at either the body structures and function level or the activities levels on the ICF. The conspicuous Þnding here was that there were no proven effective interventions for addressing the participa-

therapy; orthopaedic surgery; parent training; phenol (intramuscular injections); play therapy; respite; seating and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highly effective prevention interventions.[186,187] There is no reason to think that this trend may decline. This Þnding has important implications for managers, knowledge brokers, and clinicians about Þnding effective and efÞcient ways for health professionals to remain up to date with the latest practice. Best available knowledge translation evidence sug-

Going forward, systematic and disciplined use of outcome measures within all specialties is required for generating new evidence and conÞrming treatment effects of commonly used interventions. Routine outcome measurement is especially important when yellow-light interventions are being applied, and could circumnavigate some of the genuine research barriers including low availability of research funds and difÞculties in assembling large homogenous samples. This recommendation is particularly vital for the Þelds of speech pathology, social work, and psychology that provide key services to children with CP, without strong evidence, as of yet, to support their practice. These professions have been overshadowed in the CP research arena until recently, when the Þeld stopped solely

performance-based or Ôtop-downÕ approaches based on

managing tone since NDT is ineffective for this indication; and despite less being known about whether NDT improves function, high-quality evidence indicates that motor leaning is superior to NDT for improving function. Consequently, there are no circumstances where any of the aims of NDT could not be achieved by a more effective treatment. Thus, on the grounds of wanting to do the best for children with CP, it is hard to rationalize a continued place for traditional NDT within clinical care.

Recommendations for research

In future, systematic review authors should assign a GRADE to the body of evidence summarized, to enable clinicians to more quickly interpret the Þndings of the review for clinical practice. For the motor learning interventions that were Ôgreen lightÕ, researchers have repeatedly called for future investigations to determine optimal dosing, to better assess the widely held belief that Ômore is betterÕ. Understanding optimal intensity of therapy is important for maximizing outcomes, accurately costing services, and offering family-friendly, achievable interventions. For all the green-light interventions, additional studies that evaluate long-term outcomes are necessary. First, because families of children with CP have life-long caregiving responsibilities, an understanding the impact of these time-intensive and expensive interventions would help with expectation management and planning for lifetime care. Second, it is unknown if some interventions continue to add an incremental beneÞt when used repeatedly over years or whether the gains are one-off and short term only. Long-term outcome data are essential for costing and optimizing the outcomes of children with CP.

For the yellow-light interventions with lower-quality evidence or a paucity of research to support effectiveness, recommendations for research include the use of individual patient meta-analyses to accelerate data aggregation; collaborations that strategize multicentre data collection to overcome sample size barriers; and the use of CP registries and single-system designs if RCTs are deemed impossible or ethically undesirable to conduct. Use of these research methodologies is advisable and appropriate across all disciplines but would have particular value if applied to the disciplines of orthopaedic surgery, speech pathology,[214–216] and social work, in order to better substantiate the important contributions these clinicians make to CP care. The CP Þeld would also beneÞt from social workers and psychologists conÞrming the assumed beneÞts of proven interventions from non-CP populations amongst children with CP.

When the whole evidence base was viewed from a global perspective, there was a startling lack of interventions available to improve childrenÕs participation within their community. Given that this has been identiÞed by many of the systematic review authors as a priority area for intervention, more research designed to measure the effects of participation interventions and funds dedicated to this end is urgently needed. Furthermore, until participation-speciÞc measures with sensitivity to change have been

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