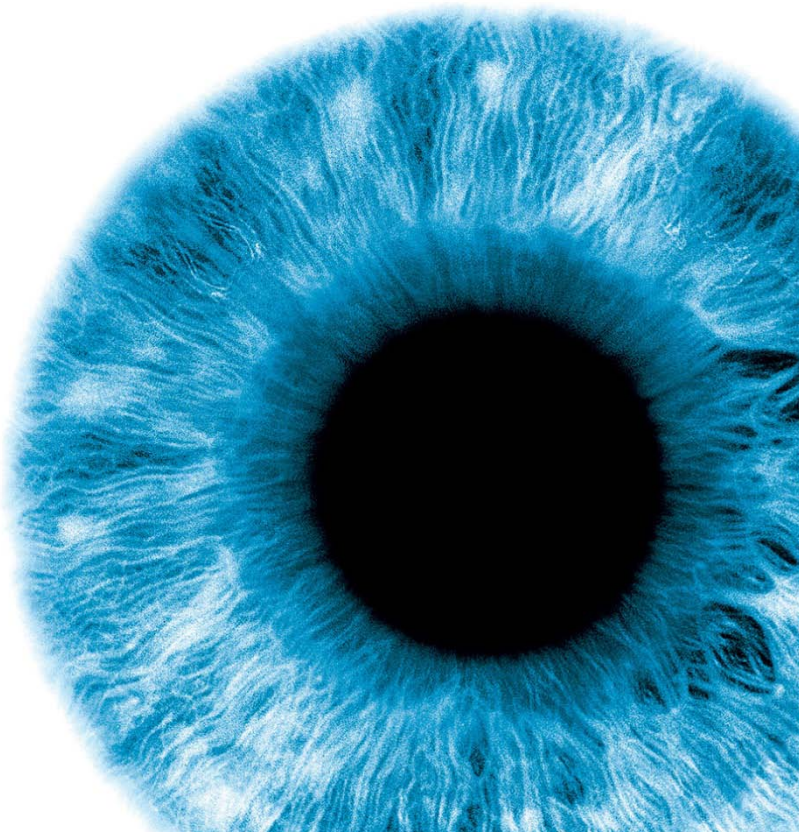
NICE National Institute for Health and Care Excellence

Spasticity in children and young people with non-progressive brain disorders

Evidence Update December 2014

A summary of selected new evidence relevant to NICE clinical guideline 'Spasticity in children and young people with non-progressive brain disorders: management of spasticity and co-existing motor disorders and their early musculoskeletal complications' (2012)

Evidence Update 70



Contents

Introduction

Evidence Updates are intended to increase awareness of new evidence – they do not replace current NICE guidance and do not provide formal practice recommendations.

Evidence Updates reduce the need for individuals, managers and commissioners to search for new evidence. For contextual information, this Evidence Update should be read in conjunction with the relevant clinical guideline.

This Evidence Update provides a summary of selected new evidence published since the literature search was last conducted for the following NICE guidance:

[1] **Spasticity in children and young people with non-progressive brain disorders. NICE clinical guideline 145 (2012)**

A search was conducted for new evidence from 8 August 2011 to 30 June 2014. A total of 1946 pieces of evidence were initially identified. After removal of duplicates, a series of automated and manual sifts were conducted to produce a list of the most relevant references. The remaining 20 references underwent a rapid critical appraisal process and then were reviewed by an Evidence Update Advisory Group, which advised on the final list of 7 items selected for the Evidence Update. See Appendix A for details of the evidence search and selection process.

Evidence selected for inclusion in this Evidence Update may highlight a potential impact on guidance: that is, a high-quality study, systematic review or meta-analysis with results that suggest a change in practice. Evidence that has no impact on guidance may be a key read, or may substantially strengthen the evidence base underpinning a recommendation in the NICE guidance.

The Evidence Update gives a preliminary assessment of changes in the evidence base and a final decision on whether the guidance should be updated will be made by NICE according to its published processes and methods.

This Evidence Update was developed to help inform the review proposal on whether or not to update NICE clinical guideline 145 (NICE CG145). The process of updating NICE guidance is separate from both the process of an Evidence Update and the review proposal.

See the NICE clinical guideline development methods for further information about updating clinical guidelines.

Other relevant NICE guidance

The focus of the Evidence Update is on the guidance stated above. However, other relevant NICE guidance has been identified as part of the Evidence Update process:

[1] Cerebral palsy. NICE clinical guideline in development (due October 2016)

NICE Pathways

NICE Pathways bring together all related NICE guidance and associated products on the condition in a set of interactive topic-based diagrams. The following NICE Pathways cover advice and recommendations related to this Evidence Update:

- Spasticity in children and young people. NICE Pathway

[1] NICE-accredited guidance

Feedback

If you would like to comment on this Evidence Update, please email contactus@evidence.nhs.uk.

Key points

The following table summarises the key points for this Evidence Update and indicates whether the new evidence may have a potential impact on NICE clinical guideline 145 (NICE CG145). Please see the full commentaries for details of the evidence informing these key points.

The section headings used in the table below are taken from NICE CG145.

Evidence Updates do not replace current NICE guidance and do not provide formal practice recommendations.

	Potential impact on guidance	
Key point	**Yes**	**No**
Physical therapy (physiotherapy and/or occupational therapy) • Physical therapy with standing programmes appears to improve range of joint motion, hip biomechanics, spasticity and bone mineral density in children and young people with cerebral palsy or other disorders affecting mental or physical development.		✓
• Intensive physical therapy using temporary restraint of an unaffected arm to encourage use of the other arm (constraint-induced movement therapy) and therapy allowing unrestrained use of both arms (intensive bimanual therapy) appear to have short-term and medium-term beneficial effects on hand function and functional movement in children with hemiplegic cerebral palsy.		✓
• An intensive programme of treadmill training without body weight support appears to improve gross motor function and walking speed in ambulatory young people with cerebral palsy.		✓
Orthoses • In young ambulatory children with cerebral palsy, wearing ankle–foot orthoses day and night appears to have no greater effect on ankle range of motion than day wear only. Day and night wear appears to have less of a beneficial effect on motor function than wearing the orthoses in the day only.		✓
Botulinum toxin type A • Early non-operative intervention with botulinum toxin type A[2] injections and abduction bracing in children with cerebral palsy who are at risk of hip displacement does not appear to improve long-term hip development compared with standard care or reduce the need for surgery.		✓

[2] At the time of publication of this Evidence Update, some botulinum toxin type A products had UK marketing authorisation for use in the treatment of focal spasticity in children, young people and adults, including the treatment of dynamic equinus foot deformity due to spasticity in ambulant paediatric cerebral palsy patients, 2 years of age or older. Other products had UK marketing authorisation only for use on the face in adults or for post-stroke spasticity of the upper limb in adults. Botulinum toxin units are not interchangeable from one product to another. Details of licensed indications and doses for individual products are available at the electronic Medicines Compendium. Where appropriate, informed consent should be obtained and documented.

Key point	Potential impact on guidance	
	Yes	No
Areas not currently covered by NICE CG145 • Limited evidence suggests that tizanidine[3] appears to be more effective than placebo at reducing spasticity in children with cerebral palsy.		✓

[3] At the time of publication of this Evidence Update, tizanidine did not have UK marketing authorisation for this indication in children and young people and was not considered by NICE CG145.

1 Commentary on new evidence

These commentaries focus on the 'key references' identified through the search process and prioritised by the EUAG for inclusion in the Evidence Update, which are shown in bold text. Supporting references provide context or additional information to the commentary. Section headings are taken from NICE clinical guideline 145 (NICE CG145).

1.1 Principles of care

No new key evidence for this section was selected for inclusion in this Evidence Update.

1.2 Physical therapy (physiotherapy and/or occupational therapy)

NICE CG145 recommends that all children and young people with spasticity referred to a network team should be promptly assessed by a physiotherapist and, where necessary, an occupational therapist. Children and young people should be offered a physical therapy (physiotherapy and/or occupational therapy) programme tailored to their individual needs and aimed at specific goals, such as:

- enhancing skill development, function and ability to participate in everyday activities
- preventing consequences such as pain or contractures.

Postural management strategies

NICE CG145 recommends considering including in the physical therapy programme 24-hour postural management strategies to:

- prevent or delay the development of contractures or skeletal deformities in children and young people at risk of developing these
- enable the child or young person to take part in activities appropriate to their stage of development.

NICE CG145 adds that when using 24-hour postural management strategies, low-load active stretching or low-load passive stretching should be considered on an individual basis. Additionally, a research recommendation states that further research is needed to compare the effectiveness of different durations and frequencies of standing frame use in postural management programmes for children aged 1–3 years.

Paleg et al. (2013) did a systematic review of duration and frequency of paediatric supported standing programmes. The population was children and young people up to the age of 21 years with atypical development, with or without a neuromuscular diagnosis (including cerebral palsy), who used a standing frame or similar device. The review described 30 studies that met these inclusion criteria; meta-analysis was not undertaken.

Four studies in children with cerebral palsy (n=122) showed that standing for 45–90 minutes a day, 3–7 times a week, improved the range of motion in the hip, knee and ankle. Standing for 30–90 minutes a day in 55–70° of total bilateral hip abduction, 5–7 times a week, appeared to improve hip biomechanics in children with cerebral palsy (4 studies, n=362). One study (n=97) that directly addressed duration and frequency of standing programmes found that weight bearing for 30–90 minutes a day, 5 days a week, stabilised hip migration after surgery.

Two studies (n=28) showed that using a traditional standing frame for 30–45 minutes, either as a one-off session or 3 times a week, reduced lower extremity spasticity or muscle tone in children with cerebral palsy. Several studies indicated that standing improved bone mineral

density at various sites, with the durations tested ranging from 9 minutes to 2 hours a day, 4–5 times a week (8 studies in children with cerebral palsy [n=170] and 2 in children with developmental delay or disabling conditions [n=42]).

The authors noted that in several of the studies of bone mineral density, the time spent standing (less than 60 minutes a day) may not have been long enough to affect bone structure. Other limitations included the small volume of evidence available that directly compared strategies of differing duration or frequency and the poor quality of the evidence for other outcomes, such as the effects of standing programmes on body functions.

This evidence suggests that physical therapy with standing programmes appears to improve range of joint motion, hip biomechanics, spasticity and bone mineral density in children and young people with cerebral palsy or other disorders affecting mental or physical development. NICE CG145 recommends considering including 24-hour postural management strategies in the physical therapy programme for children and young people with spasticity and non-progressive brain disorders. As such, this evidence is unlikely to have an impact on NICE CG145.

Key reference

Paleg GS, Smith BA, Glickman LB (2013) Systematic review and evidence-based clinical recommendations for dosing of pediatric supported standing programs. Pediatric Physical Therapy 25: 232–47

Task-focused active-use therapy in the upper limbs

NICE CG145 recommends that healthcare professionals should consider task-focused active-use therapy such as constraint-induced movement therapy (CIMT; that is, temporary restraint of an unaffected arm to encourage use of the other arm) followed by bimanual therapy (unrestrained use of both arms) to enhance manual skills. When undertaking task-focused active-use therapy, an intensive programme over a short time period (for example, 4–8 weeks) should be considered.

Hsin et al. (2012) did a randomised controlled trial testing CIMT against traditional rehabilitation in children with hemiplegic cerebral palsy and mild-to-moderate impairment in hand function. A total of 23 children aged 6–8 years were recruited from a tertiary medical centre in Taiwan and randomly allocated to CIMT (n=11) or traditional rehabilitation (n=12). The assigned treatment was individualised and administered at home for 3.5–4 hours twice a week for 4 weeks. CIMT comprised functional training of the more affected arm at relatively moderate intensity, with the less affected arm restrained with an elastic bandage and glove. The traditional rehabilitation group undertook functional unilateral or bilateral arm training. Participants in both groups were encouraged to exercise or perform daily activities at home during the study period, and those in the CIMT group were encouraged to wear the restraint equipment for 3.5–4 hours a day during these activities. Upper limb skill was measured at baseline, immediately after treatment completion and at 3 months after treatment using subtest 8 of the Bruininks–Oseretsky Test of Motor Proficiency.

A total of 22 children (n=11 in each group) completed the study. Children in the CIMT group wore the restraint equipment on average 3.5 hours a day (standard deviation [SD]=0.1 hours a day). Improvements in upper limb motor skill were seen immediately after treatment in both the CIMT group (mean change=5.4) and the rehabilitation group (mean change=4.4). Improvements were maintained at 3-month follow-up in both groups (CIMT group: mean change=7.4; rehabilitation group: mean change=5.7). The improvement was significantly greater in the CIMT group than in the rehabilitation group at both time points ($p<0.001$ for both).

This study is limited by its small sample size and the duration of treatment used, which is higher than would generally be used in the UK. In addition, the study excluded children with

more severely affected hand function, which limits the applicability of these findings to all children with cerebral palsy and the Bruininks–Oseretsky test is not commonly used in the NHS.

A randomised controlled trial by **Gordon et al. (2011)** compared CIMT with hand–arm intensive bimanual therapy in children with hemiplegic cerebral palsy. This US study randomly assigned 44 children aged 3.5–10 years to 90 hours (6 hours a day for 15 consecutive week days) of CIMT or hand–arm intensive bimanual therapy (HABIT). Both interventions comprised age-appropriate fine motor and gross motor activities, performed with the most-affected hand only in the CIMT group (participants' less-affected hand was restrained with a sling) and with both hands in the HABIT group. Children participated in whole-task, part-task and practice. Whole-task practice comprised sequencing successive movements required for specific tasks, and part-task practice involved completing the individual movements separately. Caregivers were instructed to encourage participants to practice these activities at home for 1 hour a day during and for 6 months after the intervention. Participants' hand movement and functional ability were tested using the Assisting Hand Assessment (AHA) and the Jebsen–Taylor Test of Hand Function (JTTHF), respectively, before treatment, within 2 days of completing treatment, and 1 and 6 months after treatment.

A total of 42 children completed all 90 hours of treatment and 6 months of follow-up (n=21 in each group). Children on average did 286 minutes a week of home practice (out of the 360 minutes a week requested) during the 6 month follow-up. Improvements in hand movement were seen immediately after the intervention in both the CIMT group (difference in Assisting Hand Assessment scaled logit score: 0.42 points, 95% CI 0.08 to 0.76 points) and the HABIT group (0.56 points, 95% CI 0.23 to 0.90 points) that were maintained at 6 months. Likewise both groups had improvements in hand function after completing the intervention (difference in Jebsen–Taylor Test of Hand Function score: –141.7 seconds, 95% CI –195.4 to –88.0 seconds in the CIMT group and –131.2 seconds, 95% CI –185.0 to –77.5 seconds in the HABIT group) and at 6 months. These improvements were significantly different from baseline but not between groups.

Limitations of this evidence include that the measures used may not have been sensitive enough to detect subtle changes in outcome and the treatments might be less effective if given for less than 90 hours. In addition, the study did not include a no treatment group or a usual and customary care group and that the sample size was small.

Taken together, this evidence suggests that intensive physical therapy using temporary restraint of an unaffected arm to encourage use of the other arm (CIMT) and therapy allowing unrestrained use of both arms (intensive bimanual therapy) appear to have short-term and medium-term beneficial effects on hand function and functional movement in children with hemiplegic cerebral palsy. NICE CG145 recommends both constraint-induced movement therapy and bimanual therapy as forms of active-use therapy to treat spasticity in children and young people. These two pieces of evidence are consistent with NICE CG145.

Key reference

Gordon AM, Hung YC, Brandao M et al. (2011) Bimanual training and constraint-induced movement therapy in children with hemiplegic cerebral palsy: a randomized trial. Neurorehabilitation & Neural Repair 25: 692–702

Hsin YJ, Chen FC, Lin KC et al. (2012) Efficacy of constraint-induced therapy on functional performance and health-related quality of life for children with cerebral palsy: a randomized controlled trial. Journal of Child Neurology 27: 992–9

Task-focused active-use therapy in the lower limbs

NICE CG145 recommends considering an intensive programme of task-focused active-use therapy over a short time period (for example, 4–8 weeks) to improve upper limb function in children and young people with non-progressive brain disorders and spasticity. The guideline does not make any recommendations on task-focused active-use therapy for lower limb function. Muscle-strengthening therapy should be considered where muscle weakness is contributing to loss of function or postural difficulties.

Chrysagis et al. (2012) undertook a randomised controlled trial to assess the effects of treadmill training in ambulatory young people with spastic cerebral palsy. Young people aged 13–19 years with diplegic or tetraplegic cerebral palsy (Gross Motor Function Classification System [GMFCS] levels I–III) were recruited from a special school for children with physical disabilities in Greece. Participants were randomly assigned to treadmill training without body weight support or conventional physiotherapy, both of which were delivered 3 times a week for 12 weeks. The training comprised 10-minutes of static stretching (warm up), a maximum of 30 minutes of treadmill walking, and a further 5-minutes of stretching (cool down). Speed was increased during sessions, and each session would start at the maximum speed achieved in the previous session. Gait pattern was corrected manually (from the pelvis) and verbally. The primary outcomes were gross motor function, measured using dimensions D and E of the Gross Motor Function Measure (GMFM), and self-selected walking speed over 10 metres.

A total of 22 young people (n=11 in each group) were enrolled in and finished this study, completing on average 29.45 out of 34 sessions (2 sessions were cancelled). Both groups showed improvements in gross motor function and self-selected walking speed at the end of the 12-week intervention period, although the difference from baseline was significantly larger in the treadmill group than in the conventional physiotherapy group. GMFM increased by 3.86 percentage points after treatment in the treadmill group, whereas the improvement was 0.68 percentage points in the conventional physiotherapy group (p=0.007). The improvement in walking speed was 10.26 metres/min in the treadmill group and 0.48 metres/min in the conventional physiotherapy group (p=0.009).

This evidence is limited by fact that many of the functional elements in domains D and E of the GMFM were part of the conventional physiotherapy, which means that the study may have underestimated the effects of treadmill training. In addition, it is not clear how improvements in walking on a treadmill would translate to everyday walking. Finally, the study lacked follow-up post-intervention and had a small sample size.

This evidence indicates that an intensive programme of treadmill training without body weight support appears to improve gross motor function and walking speed in ambulatory young people with cerebral palsy. Further research is needed on the longer term effects of treadmill training on gross motor function and walking speed and the optimum frequency and duration of treatment in ambulatory young people with cerebral palsy.

NICE CG145 recommends an intensive programme of task-focused active-use therapy over a short time period (for example, 4–8 weeks) to enhance manual skills. However, the recommendations in NICE CG145 focus on the upper body, whereas this research provides evidence to support the use of task-focused active-use therapy for the lower body. This evidence supports the recommendations in NICE CG145 and emphasises the efficacy of intensive physical therapy for all aspects of movement in children and young people with cerebral palsy.

Key reference

Chrysagis N, Skordilis EK, Stavrou N et al. (2012) The effect of treadmill training on gross motor function and walking speed in ambulatory adolescents with cerebral palsy: a randomized controlled trial. American Journal of Physical Medicine & Rehabilitation 91: 747–60

1.3 Orthoses

NICE CG145 recommends considering ankle–foot orthoses for children and young people with serious functional limitations (GMFCS level IV or V) to improve foot position for sitting, transfers between sitting and standing, and assisted standing. For children and young people with abnormal ankle plantar flexion that impairs their gait, consider a solid ankle–foot orthosis if they have poor control of knee or hip extension or a hinged ankle–foot orthosis if they have good control of knee or hip extension.

Children and young people who are about to start using an orthosis, and their parents or carers, should be informed that an orthosis designed to maintain stretch to prevent contractures is more likely to be effective if worn for longer periods of time, for example at least 6 hours a day. The overnight use of orthoses can be considered to improve posture, prevent or delay hip migration, or prevent or delay contractures. If an orthosis is used overnight, check that it is acceptable to the child or young person, does not cause injury and does not disturb sleep.

Zhao et al. (2013) did a randomised controlled trial of day and night wear of ankle–foot orthoses compared with day wear only in ambulatory children with cerebral palsy. Children aged 1–4 years with diplegic cerebral palsy (GMFCS levels I and II) were recruited from a single hospital in China and were randomly assigned to day and night wear or day wear only of plastic, custom-made, hinged ankle–foot orthoses. Children assigned to the day–night group wore the orthoses during the day and night for almost 24 hours, whereas those assigned to the day group wore the orthoses during the day for 6–12 hours and not at night. Both groups received conventional physiotherapy 5 times a week for the 8-week study period. The primary outcomes were change from baseline in passive ankle dorsiflexion and in gross motor function (measured using dimensions D and E of the GMFM).

A total of 112 children were randomly assigned to day–night wear of orthoses (n=56) or day wear of orthoses only (n=56); 52 and 53 children, respectively, completed the study. Children in the day–night group wore their orthoses for an average of 19.4 hours every day, compared with 6.8 hours in the day group. Both groups had a significant improvement in ankle range of motion at the end of the 8-week study period. The day–night group showed a mean improvement in ankle dorsiflexion of 3.83 (95% CI 3.12 to 4.54, $p<0.001$), whereas the improvement was 3.62 (95% CI 2.94 to 4.31, $p<0.001$) in the day group ($p=0.68$ for between-group comparison). Both groups also showed significant improvements in gross motor function, by 11.68 points on the GMFM (95% CI 10.33 to 13.03 points, $p<0.001$) in the day–night group and 14.92 points (95% CI 13.40 to 16.45 points, $p<0.001$) in the day group. The improvement in motor function in the day group was significantly greater than that in the day–night group (mean difference=3.26, 95% CI 1.26 to 5.27, $p<0.01$).

Limitations of the study include the use of conventional physiotherapy in both groups, which may have been a confounding factor. In addition, the children in this study were young (mean age=30.66 months in the day–night group and 31.20 months in the day group) and had mild-to-moderate cerebral palsy (GMFCS levels I and II), so the results cannot be generalised to all children with cerebral palsy. The authors looked only at the immediate effects of the orthoses straight after completion of the intervention and not the long-term effects.

This evidence shows that in young ambulatory children with cerebral palsy, wearing ankle–foot orthoses day and night appears to have no greater effect on ankle range of motion than day wear only. Day and night wear appears to have less of a beneficial effect on motor function than wearing the orthoses in the day only. NICE CG145 recommends considering ankle–foot orthoses in children and young people with serious functional limitations (GMFCS level IV or V) and in children with abnormal ankle plantarflexion. It adds that the overnight use of orthoses should be considered to improve posture, prevent or delay hip migration,

or prevent or delay contractures, but makes no recommendations on the overnight use of ankle–foot orthoses to improve function. Given that this study is in a very specific population (children aged 1–4 years with GMFCS level I or II), this evidence is unlikely to have an impact on NICE CG145.

Key reference

Zhao X, Xiao N, Li H et al. (2013) Day vs. day-night use of ankle-foot orthoses in young children with spastic diplegia: a randomized controlled study. American Journal of Physical Medicine & Rehabilitation 92: 905–11

1.4 Oral drugs

No new key evidence for this section was selected for inclusion in this Evidence Update.

1.5 Botulinum toxin type A

NICE CG145 recommends considering botulinum toxin type A[4] treatment where focal spasticity of the lower limb is impeding gross motor function or impeding tolerance of other treatments, such as orthoses and use of equipment to support posture. After treatment with botulinum toxin type A, an orthosis should be considered to enhance stretching of the temporarily weakened muscle and to enable the child or young person to practice functional skills.

NICE CG145 adds that orthopaedic surgery should be considered an important adjunct to other interventions in the management programme for some children and young people with spasticity. An assessment should be performed by an orthopaedic surgeon within the network team if there is concern, on the basis of clinical findings or radiological monitoring, that the child or young person's hip may be displaced. Assessment should also take place if the child or young person has hip migration greater than 30% or hip migration percentage increasing by more than 10 percentage points per year.

Willoughby et al. (2012) did a long-term follow-up of an Australian randomised controlled trial that assessed the effects of regular botulinum toxin type A injections and abduction bracing on hip development and need for surgery in children with cerebral palsy. The original randomised controlled trial (Graham et al. 2008) tested 6-monthly botulinum toxin type A injections for 3 years, combined with hip abduction bracing, versus standard care and surveillance in 91 children with bilateral spastic cerebral palsy. All participants were aged 1–5 years at study enrolment and were at risk of hip displacement, with a hip migration percentage of 10–40%. At the end of the 3-year study period, the rate of hip displacement and surgery was lower in the intervention group than in the standard care group, but both groups continued to report hip displacement.

The present analysis followed up 46 of these children (n=23 in each study group) from 1 of the 4 study centres. The primary outcomes were hip migration percentage and morphology, as judged from the most recent hip radiograph. Need for preventive or reconstructive surgery was assessed using chart review of hip surveillance and orthopaedic department records.

[4] At the time of publication of this Evidence Update, some botulinum toxin type A products had UK marketing authorisation for use in the treatment of focal spasticity in children, young people and adults, including the treatment of dynamic equinus foot deformity due to spasticity in ambulant paediatric cerebral palsy patients, 2 years of age or older. Other products had UK marketing authorisation only for use on the face in adults or for post-stroke spasticity of the upper limb in adults. Botulinum toxin units are not interchangeable from one product to another. Details of licensed indications and doses for individual products are available at the electronic Medicines Compendium. Where appropriate, informed consent should be obtained and documented.

At a mean of 10 years and 10 months from study entry, no difference was seen between the botulinum toxin type A and bracing group and the standard care group in hip migration or morphology. The mean percentage hip migration was 15.9% in the intervention group and 15.2% in the standard care group (p=0.79), and most children in both groups had 'satisfactory' hip morphology (Melbourne Cerebral Palsy Hip Classification System grades I–III, p=0.11). A similar number of children in both groups needed preventive or reconstructive surgery, or both, during long-term follow-up. Overall, 21 (91%) children in the intervention group needed preventive surgery and 10 (43%) needed reconstructive surgery; these values were 19 (83%) and 8 (35%), respectively, in the standard care group. However, botulinum toxin type A injections and abduction bracing did delay the need for surgery in the intervention group by an average of 18 months compared with the standard care group, although this difference was not significant.

This study was limited by the lack of outcome measures of function, activity and participation. In addition, this study had an observational follow-up design and took place at a single centre, limiting its validity. The analysis did not adjust for confounding factors, and it is not possible to distinguish the effects of the botulinum toxin type A injections from those of the abduction bracing.

This evidence shows that early non-operative intervention with botulinum toxin type A injections and abduction bracing in children with cerebral palsy who are at risk of hip displacement does not appear to improve long-term hip development compared with standard care or reduce the need for surgery. NICE CG145 recommends considering botulinum toxin type A treatment for focal spasticity of the lower limb, and suggests timely orthopaedic surgery as an adjunct treatment in children and young people at risk of hip displacement. Given the limitations of this study, this evidence is unlikely to have an impact on NICE CG145.

Key reference

Willoughby K, Ang SG, Thomason P et al. (2012) The impact of botulinum toxin A and abduction bracing on long-term hip development in children with cerebral palsy. Developmental Medicine & Child Neurology 54: 743–7

Supporting reference

Graham HK, Boyd R, Carlin JB et al. (2008) Does botulinum toxin A combined with bracing prevent hip displacement in children with cerebral palsy and "hips at risk"? A randomized, controlled trial. The Journal of Bone & Joint Surgery 90: 23–33

1.6 Intrathecal baclofen

No new key evidence for this section was selected for inclusion in this Evidence Update.

1.7 Orthopaedic surgery

No new key evidence for this section was selected for inclusion in this Evidence Update.

1.8 Selective dorsal rhizotomy

No new key evidence for this section was selected for inclusion in this Evidence Update.

Areas not currently covered by NICE CG145

Oral tizanidine

NICE CG145 recommends considering oral diazepam or oral baclofen in children and young people if at least one of several spasticity-related criteria is met. The full version of NICE CG145 notes that several other oral drugs were considered in the guideline development

process, including tizanidine[5]. No evidence was found comparing tizanidine with placebo or comparing tizanidine with baclofen, alone or with dantrolene[5].

A randomised controlled trial in Iran by **Nikkhah et al. (2011)** compared tizanidine with placebo in children with cerebral palsy. Children aged 2–14 years with hemiplegic cerebral palsy were recruited from a single centre in Iran and randomly assigned to either tizanidine (2 mg/day for children aged under 7 years and 4 mg/day for children aged more than 7 years) or a matching placebo. The primary outcome was change in spastic hypertonia, assessed using the Modified Ashworth Scale at baseline and at the end of the 2-week treatment period.

A total of 60 children (n=30 in each group) with a mean age of 7.3 years were included in the study. At the end of the 2-week treatment period, 15 (50%) of children who received tizanidine had an improvement in spastic hypertonia on the affected side, compared with 2 (6.7%) in the placebo group ($p<0.0001$). In addition, a greater proportion of children or parents in the tizanidine group than in the placebo group reported a reduction in pain on the child's affected side at the end of the study (66.7% versus 13.3%, $p<0.0001$). No serious adverse effects were reported.

This study was limited by the lack of information on randomisation, allocation concealment and blinding. The sample size was relatively small (n=60), and follow-up was short (2 weeks). In addition, the functional abilities of the children was not well described, the degree of change in Modified Ashworth Scale in each group was not reported, and the method of assessing pain was not well described. Although the authors reported that no serious side effects were observed, the side effects were not listed.

Limited evidence suggests that tizanidine appears to be more effective than placebo at reducing spasticity in children with cerebral palsy. NICE CG145 does not make any recommendations on the use of tizanidine to manage spasticity in children and young people with non-progressive brain disorders. However, the shortcomings of this study, plus the fact that tizanidine is not licenced in the UK for children and young people under the age of 18 years, mean that this evidence is unlikely to have an impact on NICE CG145. Further research is needed to assess the efficacy of tizanidine compared with existing treatments, such as baclofen, and to confirm the safety of the drug in children and young people.

Key reference

Nikkhah A, Mohammadi M, Ashrafi MR et al. (2011) The efficacy and safety of tizanidine in treating spasticity in children with cerebral palsy. Iranian Journal of Child Neurology 5: 19–22

[5] At the time of publication of this Evidence Update, tizanidine and dantrolene did not have UK marketing authorisation for this indication in children and young people and were not considered by NICE CG145.

2 New evidence uncertainties

During the development of the Evidence Update, the following evidence uncertainties were identified for the UK Database of Uncertainties about the Effects of Treatments (UK DUETs).

Physical therapy (physiotherapy and/or occupational therapy)

- The effect of treadmill training on gross motor function and walking speed in ambulatory adolescents with cerebral palsy.

Areas not currently covered by NICE CG145

- The efficacy and safety of tizanidine in treating spasticity in children with cerebral palsy.

Further evidence uncertainties for spasticity in children and young people can be found in the UK DUETs database and in the NICE research recommendations database.

UK DUETs was established to publish uncertainties about the effects of treatments that cannot currently be answered by referring to reliable up-to-date systematic reviews of existing research evidence.

Appendix A: Methodology

Scope

The scope of this Evidence Update is taken from the scope of the reference guidance:

- Spasticity in children and young people with non-progressive brain disorders. NICE clinical guideline 145 (2012)

Searches

The literature was searched to identify studies and reviews relevant to the scope. Searches were conducted of the following databases, covering the dates 8 August 2011 (the end of the search period of NICE CG145) to 30 June 2014:

- AMED (Allied and Complementary Medicine Database)
- CDSR (Cochrane Database of Systematic Reviews)
- CENTRAL (Cochrane Central Register of Controlled Trials)
- CINAHL (Cumulative Index to Nursing and Allied Health Literature)
- DARE (Database of Abstracts of Reviews of Effects)
- EMBASE (Excerpta Medica database)
- HTA (Health Technology Assessment) database
- MEDLINE (Medical Literature Analysis and Retrieval System Online)
- MEDLINE In-Process
- NHS EED (Economic Evaluation Database)
- PsycINFO

The Evidence Update search strategy replicates the strategy used by NICE CG145 (for key words, index terms and combining concepts) as far as possible. Where necessary, the strategy is adapted to take account of changes in search platforms and updated indexing language.

The searches for NICE CG145 were undertaken using slightly different population terms for each review question. For this Evidence Update, all the variations in population search terms were combined into a single inclusive strategy.

Validated Scottish Intercollegiate Guidelines Network search filters for systematic reviews, randomised controlled trials and observational studies were used across all searches for this Evidence Update. In addition, a search filter was applied for children and young people, based on a published, validated filter (the Cochrane childhood cancer group filter; Table 1).

Table 2 provides details of the MEDLINE search strategy used, which was adapted to search the other databases listed above.

Figure 1 provides details of the evidence selection process. The list of evidence excluded after review by the Chair of the EUAG, and the full search strategies, are available on request from contactus@evidence.nhs.uk

See the NICE Evidence Services website for more information about how NICE Evidence Updates are developed.

Table 1 Children and young people search filter

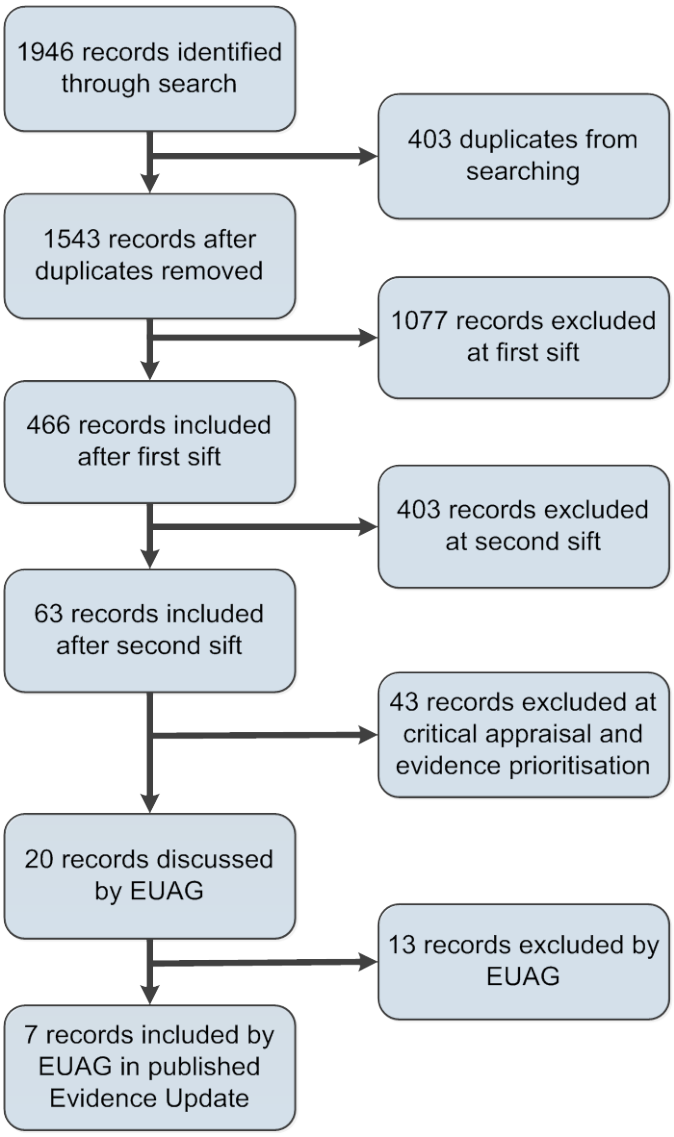
1	Infan*.mp,so.
2	newborn*.mp,so.
3	new-born*.mp,so.
4	perinat*.mp,so.
5	neonat*.mp,so.
6	baby*.mp,so.
7	babies.mp,so.
8	toddler*.mp,so.
9	minor.mp,so.
10	minors*.mp,so.
11	boy.mp,so.
12	boys.mp,so.
13	boyfriend.mp,so.
14	boyhood.mp,so.
15	girl*.mp,so.
16	kid.mp,so.

17	kids.mp,so.
18	child*.mp,so.
19	adolescen*.mp,so.
20	juvenil*.mp,so.
21	youth*.mp,so.
22	teen*.mp,so.
23	under*age*.mp,so.
24	pubescen*.mp,so.
25	exp pediatrics/
26	pediatric*.mp,so.
27	paediatric*.mp,so.
28	peadiatric*.mp,so.
29	school*.mp,so.
30	prematur*.mp,so.
31	preterm*.mp,so.
32	or/1-32

Table 2 MEDLINE search strategy (adapted for individual databases)

1	MUSCLE SPASTICITY/
2	exp SPASM/
3	exp MUSCLE HYPERTONIA/
4	(spastic$ or spasm$).ti,ab.
5	hyperton$.ti,ab.
6	exp DYSKINESIAS/
7	dyskinesi$.ti,ab.
8	((abnormal$ or involuntar$) adj2 mov$).ti,ab.
9	exp DYSTONIA/
10	dystoni$.ti,ab.
11	exp CHOREA/
12	(chorea$ or choreic$ or choreo$).ti,ab.
13	exp ATHETOSIS/
14	(athetos$ or athetoid).ti,ab.
15	MUSCLE WEAKNESS/
16	(musc$ adj3 weak$).ti,ab.
17	exp ATAXIA/
18	atax$.ti,ab.
19	upper motor neuron? lesion$.ti,ab.
20	or/1-19
21	exp BRAIN INJURIES/
22	((non progressive or non?progressive or acquired) adj2 brain injur$).ti,ab.
23	ABI.ti,ab.
24	static encephalopath$.ti,ab.
25	CEREBRAL PALSY/
26	(cerebral adj3 pals$).ti,ab.
27	exp MENINGITIS/
28	(meningitis or meningococcal).ti,ab.
29	exp CRANIOCEREBRAL TRAUMA/
30	((head or brain or skull or cerebral or craniocerebral) adj3 (injur$ or trauma$ or damage$ or disturb$ or insult$)).ti,ab.
31	exp ENCEPHALITIS/
32	encephaliti$.ti,ab.
33	exp STROKE/
34	stroke$.ti,ab.
35	((brain or cerebral or intra cranial or intra?cranial) adj3 (embolism or aneurysm$ or isch?emi$)).ti,ab.
36	exp CEREBROVASCULAR DISORDERS/
37	((brain vascular or intra cranial vascular or intra?cranial vascular or cerebrovascular) adj2 (disorder$ or disease$ or insufficien$ or occlusion$ or damage$ or disturb$ or insult$)).ti,ab.
38	exp HYDROCEPHALUS/
39	hydrocephal$.ti,ab.
40	SHAKEN BABY SYNDROME/
41	(shak$ adj3 (injur$ or syndrome$)).ti,ab.
42	or/21-41
43	exp PARALYSIS/
44	HEMIPLEGIA/
45	exp PARAPLEGIA/
46	QUADRIPLEGIA/
47	exp PARESIS/
48	(monoplegi$ or diplegi$ or hemiplegi$ or quadriplegi$ or tetraplegi$).ti,ab.
49	(monopares$ or dipares$ or hemipares$ or quadripares$ or tetrapares$).ti,ab.
50	(unilateral$ or bilateral$).ti,ab.
51	or/43-50
52	and/20,51
53	and/42,51
54	and/20,42
55	or/52-54
56	limit 55 to (english language and yr="2011 -Current")

Figure 1 Flow chart of the evidence selection process



EUAG – Evidence Update Advisory Group

Appendix B: The Evidence Update Advisory Group and Evidence Update project team

Evidence Update Advisory Group

The Evidence Update Advisory Group is a group of topic experts who reviewed the prioritised evidence from the literature search and advised on the development of the Evidence Update.

Dr Paul Eunson – Chair

Consultant Paediatric Neurologist, Royal Hospital for Sick Children, Edinburgh

Dr Gordon Allan

General Practitioner, Fife

Dr Lucinda Carr

Consultant Paediatric Neurologist, Great Ormond Street Hospital for Children, London

Ms Stephanie Cawker

Clinical Specialist Physiotherapist in Neuro-disabilities, Great Ormond Street Hospital for Children, London

Ms Tina Gericke

Paediatric Occupational Therapist, Royal Hampshire County Hospital (retired)

Mr Alec Musson

Clinical Service Manager – Children's Physiotherapy, Leeds Children's Hospital

Mr James Robb

Orthopaedic Surgeon, University of St Andrews

Evidence Update project team

Marion Spring

Associate Director

Dr Chris Alcock

Clinical Lead

Cath White

Programme Manager

Fran Wilkie

Project Manager

Helen Jaques

Medical Writer

Bazian

Information Specialist support