4-year surveillance (2016)

Spasticity in under 19s: management (2012) NICE guideline CG145

Appendix A: Summary of new evidence from surveillance

Principles of care

145 – 01 Principles of care

Recommendations derived from this question

Delivering care

1.1.1 Children and young people with spasticity should have access to a network of care that uses agreed care pathways supported by effective communication and integrated team working.

1.1.2 The network of care should provide access to a team of healthcare professionals experienced in the care of children and young people with spasticity. The network team should provide local expertise in paediatrics, nursing, physiotherapy and occupational therapy. Access to other expertise, including orthotics, orthopaedic surgery and/or neurosurgery and paediatric neurology, may be provided locally or regionally.

1.1.3 If a child or young person receives treatment for spasticity from healthcare professionals outside the network team, this should be planned and undertaken in discussion with the network team to ensure integrated care and effective subsequent management.

Management programmes

1.1.4 Following diagnosis, ensure that all children and young people with spasticity are referred without delay to an appropriate member of the network team.

1.1.5 Offer a management programme that is:

- developed and implemented in partnership with the child or young person and their parents or carers
- individualised
- goal focused.

1.1.6 When formulating a management programme take into account its possible impact on the individual child or young person and their family.

1.1.7 Carefully assess the impact of spasticity in children and young people with cognitive impairments:

- be aware that the possible benefit of treatments may be more difficult to assess in a child or young person with limited communication
- ensure that the child or young person has access to all appropriate services.

1.1.8 Identify and agree with children and young people and their parents or carers assessments and goals that:

- are age and developmentally appropriate
- focus on the following domains of the World Health Organization's International Classification of Functioning, Disability and Health (children and youth version):
  - body function and structure
  - activity and participation.

1.1.9 Record the child or young person's individualised goals and share these goals with healthcare professionals in the network team and, where appropriate, other people involved in their care.

1.1.10 Help children and young people and their parents or carers to be partners in developing and implementing the management programme by offering:

- relevant, and age and developmentally appropriate, information and educational materials
- regular opportunities for discussion and
- advice on their developmental potential and how different treatment options may affect this.

Supporting the child or young person and their parents or carers

1.1.11 Offer contact details of patient organisations that can provide support, befriending, counselling, information and advocacy.

1.1.12 Ensure that children and young people have timely access to equipment necessary for their management programme (for example, postural management equipment such as sleeping, sitting or standing systems).

1.1.13 The network team should have a central role in transition to prepare young people and their parents or carers for the young person's transfer to adult services.

Monitoring

1.1.14 Monitor the child or young person's condition for:

- the response to treatments
- worsening of spasticity
- developing secondary consequences of spasticity, for example pain or contractures
- the need to change their individualised goals.

1.1.15 The network of care should have a pathway for monitoring children and young people at increased risk of hip displacement.

1.1.16 Recognise the following clinical findings as possible indicators of hip displacement (hip migration greater than 30%):

- pain arising from the hip
- clinically important leg length difference
- deterioration in hip abduction or range of hip movement
- increasing hip muscle tone
- deterioration in sitting or standing
- increasing difficulty with perineal care or hygiene.

1.1.17 Offer a hip X-ray to assess for hip displacement:

- if there are clinical concerns about possible hip displacement
- at 24 months in children with bilateral cerebral palsy.

1.1.18 Consider repeating the hip X-ray annually in children or young people who are at Gross Motor Function Classification System (GMFCS) level III, IV or V.

1.1.19 Consider repeating the hip X-ray after 6 months in children and young people where the initial hip migration is greater than 30%, and then consider repeating the hip X-ray every 6 months after this if the hip migration is increasing by more than 10 percentage points per year.

Surveillance decision

This review question should not be updated.

Prevention of hip dislocation

2-year Evidence Update

No relevant evidence was identified.

4-year surveillance summary

A cohort study[1] (n=689) examined a population-based hip dislocation prevention programme.

In 1994 a cerebral palsy register and healthcare programme was established in southern Sweden with the primary aim of preventing dislocation of the hip in these children. The programme involves regular physical assessment by a physiotherapist and occupational therapist alongside x-ray surveillance. The results from the first 10 years were published in 2005 and showed a decrease in the incidence of dislocation of the hip from 8% in a historical group (control) of 103 children born 1990–1, to 0.5% in a group (study group 1) of 258 children born 1992–7. These 2 cohorts were re-evaluated and an additional group (study group 2) of 431 children born between 1998 and 2007 was added.

By January 2014, significantly more children in the control group than in study groups 1 and 2 had developed a dislocated hip. Every child with a dislocated hip reported severe pain, at least periodically, and 4 underwent salvage surgery. Of the 689 children in the study groups, 91 (13%) underwent preventive surgery.

Topic expert feedback

Topic experts highlighted the above paper. They noted that the study forms part of growing evidence about proactive surveillance and prevention of deformity being the gold standard for this group of children. It relates directly to the significant change in clinical management ongoing in the UK where the musculoskeletal surveillance programme in Scotland, Scandinavia and Australia is now being replicated in England and Wales. This is a direct result of this evidence and a significant change to clinical management. The programme is based on regular standardised objective physical assessment of ranges of movement running alongside x-ray surveillance at specified points during development, related to Gross Motor Function Classification System (GMFCS) levels. This relates directly to making changes to the physical management programme and/or onward referral for interventions. It is a broadening of the previous recommendation.

However topic experts also noted that more evidence is needed on which particular parts of the programme make the most difference, as the intensive measurements sessions involved are quite time consuming and potentially costly.

Impact statement

The new evidence suggests that a population-based hip surveillance programme involving regular physical assessment alongside x-ray surveillance can enable early identification and preventive treatment, which can lower the incidence of dislocation of the hip in children with cerebral palsy.

CG145 did not include a review question specifically examining monitoring and prevention of hip dislocation. However the full version of the guideline notes that the Guideline Committee was aware that clinical and radiological monitoring for signs of hip displacement was important to ensure timely access to orthopaedic surgery and to avoid preventable complications, and specific recommendations were made. However the recommendations were based on current practice and clinical experience rather than published evidence.

CG145 currently recommends monitoring children and young people at increased risk of hip displacement, recognising clinical findings as possible indicators of hip displacement, and regular x-rays in high risk groups. Although the new evidence suggests that adding regular physical assessment to x-ray surveillance could be beneficial in preventing hip dislocation, uncertainties over the exact nature of the effective surveillance and additional cost of the physical assessments mean that this evidence is currently unlikely to affect the guideline. This area will be monitored in future surveillance reviews.

New evidence is unlikely to change guideline recommendations.

Physical therapy (physiotherapy and/or occupational therapy)

145 – 02 What is the effectiveness of physical therapy (physiotherapy and/or occupational therapy) interventions in children with spasticity with or without other motor disorders (dystonia, muscle weakness and choreoathetosis) caused by a non progressive brain disorder?

Recommendations derived from this question

General principles

1.2.1 All children and young people with spasticity referred to the network team should be promptly assessed by a physiotherapist and, where necessary, an occupational therapist.

1.2.2 Offer a physical therapy (physiotherapy and/or occupational therapy) programme tailored to the child or young person's 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.

1.2.3 Give children and young people and their parents or carers verbal and written (or appropriate formats) information about the physical therapy interventions needed to achieve the intended goals. This information should emphasise the balance between possible benefits and difficulties (for example, time commitment or discomfort), to enable them to participate in choosing a suitable physical therapy programme.

1.2.4 When formulating a physical therapy programme for children and young people take into account:

- the views of the child or young person and their parents or carers
- the likelihood of achieving the treatment goals
- possible difficulties in implementing the programme
- implications for the individual child or young person and their parents or carers, including the time and effort involved and potential individual barriers.

1.2.5 When deciding who should deliver physical therapy, take into account:

- whether the child or young person and their parents or carers are able to deliver the specific therapy
- what training the child or young person or their parents or carers might need
- the wishes of the child or young person and their parents or carers.

1.2.6 Ensure that any equipment or techniques used in the physical therapy programme are safe and appropriate, in particular for children or young people with any of the following:

- poorly controlled epilepsy
- respiratory compromise
- increased risk of pulmonary aspiration
- increased risk of bone fracture due to osteoporosis (for example, those who are unable to walk, malnourished or taking anti-epileptic therapy).

1.2.7 Encourage children and young people and their parents or carers to incorporate physical therapy into daily activities (for example, standing at the sink while brushing teeth in order to stretch leg muscles).

Specific strategies

1.2.8 Consider 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.

1.2.9 When using 24-hour postural management strategies consider on an individual basis low-load active stretching or low-load passive stretching.

1.2.10 Offer training to parents and carers involved in delivering postural management strategies.

1.2.11 Consider task-focused active-use therapy such as constraint-induced movement therapy (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.

1.2.12 When undertaking task-focused active-use therapy consider an intensive programme over a short time period (for example, 4–8 weeks).

1.2.13 Consider muscle-strengthening therapy where the assessment indicates that muscle weakness is contributing to loss of function or postural difficulties.

1.2.14 Direct muscle-strengthening therapy towards specific goals using progressive repetitive exercises performed against resistance.

1.2.15 Following treatment with botulinum toxin type A, continuous pump-administered intrathecal baclofen, orthopaedic surgery or selective dorsal rhizotomy, provide an adapted physical therapy programme as an essential component of management.

1.2.16 Ensure that children and young people and their parents or carers understand that an adapted physical therapy programme will be an essential component of management following treatment with botulinum toxin type A, continuous pump-administered intrathecal baclofen, orthopaedic surgery or selective dorsal rhizotomy.

Continuing assessment

1.2.17 Reassess the physical therapy programme at regular intervals to ensure that:

- the goals are being achieved
- the programme remains appropriate to the child or young person's needs.

Surveillance decision

This review question should not be updated.

Postural management

2-year Evidence Update

A systematic review[2] of 30 studies (children and young people <21 years with atypical development, with or without a neuromuscular diagnosis [including cerebral palsy], who used a standing frame or similar) examined supported standing programmes. No meta-analysis was done. Standing for 45–90 minutes a day, 3–7 times a week, improved the range of motion in hip, knee and ankle. Standing for 30–90 minutes a day in 55–70° of total bilateral hip abduction, 5–7 times a week, improved hip biomechanics. Weight bearing for 30–90 minutes a day, 5 days a week, stabilised hip migration after surgery. 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. Standing (from 9 minutes to 2 hours a day, 4–5 times a week) improved bone mineral density at various sites.

4-year surveillance summary

An RCT[3] (n=30) examined the effect of backward walking training on postural balance in children aged 10–14 years with spastic hemiparetic cerebral palsy. All children received traditional physical therapy for 12 weeks, with half randomised to receive additional backward walking training for 25 minutes a day, 3 days a week for 3 months. Overall, anteroposterior, and mediolateral stability indices were evaluated using the Biodex balance system. After treatment, significant improvements in both groups were seen in all measured variables at both the most stable level (level 12) and moderately unstable level (level 7). However, the overall, anteroposterior and mediolateral stability indices were significantly more improved in the

backward walking group at both stability levels versus controls.

Topic expert feedback

No topic expert feedback was relevant to this evidence.

Impact statement

The 2-year Evidence Update found that physical therapy with standing programmes improved 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. The evidence was deemed unlikely to have an impact on CG145 which already recommends considering including 24-hour postural management strategies in the physical therapy programme.

Evidence from 4-year surveillance showed that backward walking training additional to traditional physical therapy can improve postural stability in children with spastic hemiparetic cerebral palsy. During the development of CG145, no studies were identified of backward walking nor any other postural management programmes. CG145 does not include recommendations on backward walking, however this evidence was from a single small trial therefore is unlikely to impact on the guideline at this time.

New evidence is unlikely to change guideline recommendations.

Task-focused active-use therapy in the upper limbs: constraint-induced movement therapy (CIMT) and bimanual therapy

2-year Evidence Update

An RCT[4] (n=23) compared CIMT with traditional rehabilitation in children aged 6–8 years with hemiplegic cerebral palsy and mild-to-moderate impairment in hand function. 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 moderate intensity, with the less affected arm restrained. Traditional rehabilitation was functional unilateral or bilateral arm training. Both groups were encouraged to exercise or perform daily activities at home, and the CIMT group were asked to wear the restraint for 3.5–4 hours a day during these activities. Upper limb skill was measured using subtest 8 of the Bruininks–Oseretsky Test of Motor Proficiency. Significantly greater improvements in upper limb motor skill were seen in the CIMT group versus controls immediately after treatment, which were maintained at 3-months.

An RCT[5] (n=44) compared CIMT with hand–arm intensive bimanual therapy (HABIT) in children aged 3.5–10 years with hemiplegic cerebral palsy. Both interventions were performed for 90 hours (6 hours a day for 15 consecutive week days) and both comprised age-appropriate fine motor and gross motor activities, performed with the most-affected hand only in the CIMT group (less-affected hand restrained) and with both hands in the HABIT group. Children participated in whole-task practice (sequencing successive movements required for specific tasks) and part-task practice (completing the individual movements separately). Caregivers were also instructed to engage participants in home practice 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 and the Jebsen–Taylor Test of Hand Function respectively. Significant improvements in hand movement and hand function were seen immediately after the intervention in both groups, which were maintained at 6 months, though improvements did not differ significantly between groups.

4-year surveillance summary

A systematic review and meta-analysis[6] of 27 RCTs examined the effect of CIMT on upper limb function in children with cerebral palsy. Overall, CIMT provided a 'medium' (term not defined) significant beneficial effect versus conventional therapy. In subgroup analyses, presence of a dose-equivalent comparison group, intervention location, and time of follow-up were significant factors. Studies examining CIMT without a dose-equivalent comparison group showed a 'large' effect in children with cerebral palsy, but studies with a dose-equivalent group only showed a 'small' effect. Children who received home-based CIMT had more improvement in arm function than those

receiving CIMT elsewhere (significance not stated in the abstract).

An RCT[7] (n=53) compared the effect of short-term intensive group-based therapy combining modified CIMT and bimanual therapy (hybrid-CIMT) with standard care on upper limb motor outcomes in children (mean age 7.8 years) with unilateral cerebral palsy. All children were Manual Ability Classification System level I or II. Standard care comprised 6 weekly occupational therapy sessions and a 12-week home programme. Standard care led to significantly greater gains on both satisfaction with occupational performance after the intervention, and Assisting Hand Assessment at 26 weeks. Significantly improved dexterity of the impaired upper limb, and bimanual and occupational performance over time, was seen in both groups. Differences between groups were not clinically meaningful.

Topic expert feedback

No topic expert feedback was relevant to this evidence.

Impact statement

The 2-year Evidence Update found that intensive CIMT and intensive bimanual therapy appeared to have short-term and medium-term beneficial effects on hand function and functional movement in children with hemiplegic cerebral palsy. Evidence from 4-year surveillance appears to support CIMT as an effective intervention to improve arm function in children with cerebral palsy. All the evidence is consistent with NICE CG145 that recommends considering task-focused active-use therapy such as CIMT and bimanual therapy, and considering intensive task-focused active-use programmes over a short time period (for example, 4–8 weeks).

Further evidence from 4-year surveillance found no difference between group-based hybrid-CIMT and standard care, but CG145 does not specifically recommend group therapy therefore no impact on the guideline is anticipated.

New evidence is unlikely to change guideline recommendations.

Task-focused active-use therapy in the lower limbs: treadmill training

2-year Evidence Update

An RCT[8] (n=22) assessed treadmill training without body weight support versus conventional physiotherapy in ambulatory young people aged 13–19 years with diplegic or tetraplegic cerebral palsy (GMFCS levels I−III). Both groups received their respective interventions 3 times a week for 12 weeks. Treadmill training comprised 10-minutes static stretching (warm up), 30 minutes (maximum) treadmill walking, and 5 minutes stretching (cool down). Speed was increased during sessions, and each session started at the maximum speed achieved in the previous session. Gait pattern was corrected manually (from the pelvis) and verbally. Both groups showed improvements in gross motor function and self-selected walking speed over 10 metres at the end of the intervention period, although difference from baseline was significantly larger with treadmill training than conventional physiotherapy. Gross Motor Function Measure (GMFM) increased significantly more in the treadmill than the conventional physiotherapy group. Walking speed significantly improved by almost 10 metres/min more in the treadmill group compared with the conventional physiotherapy group.

4-year surveillance summary

No relevant evidence was identified.

Topic expert feedback

No topic expert feedback was relevant to this evidence.

Impact statement

The Evidence Update found that intensive treadmill training without body weight support appeared to improve gross motor function and walking speed in ambulatory young people with cerebral palsy. 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 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 emphasises the efficacy of intensive physical therapy for all aspects of

movement in children and young people with cerebral palsy. However, the Evidence Update noted that this was a single small RCT. In order to more firmly establish the place of task-focused active-use therapy for the lower body, the Evidence Update stated that 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. Therefore this evidence is unlikely to affect the guideline.

New evidence is unlikely to change guideline recommendations.

Muscle strengthening therapy: progressive resistance training

2-year Evidence Update

No relevant evidence was identified.

4-year surveillance summary

An RCT[9] (n=36) examined the effects of individualised lower limb progressive resistance training versus usual care on daily physical activity in adolescents and young adults with bilateral spastic cerebral palsy and mild to moderate walking disabilities. Progressive resistance training was conducted twice a week for 12 weeks in community gymnasiums. At 12 weeks, there were no between-group differences for any of the daily physical activity primary outcomes (number of steps, and time sitting and lying). The secondary outcome of leg press strength was numerically higher after resistance training than usual care but did not differ significantly. No significant adverse events occurred during training.

Topic expert feedback

No topic expert feedback was relevant to this evidence.

Impact statement

The new evidence suggests that short-term progressive resistance training may have the potential to increase muscle strength, but does not appear to be effective in increasing daily physical activity in young people with bilateral spastic cerebral palsy and mild to moderate walking disabilities. CG145 recommends considering muscle-strengthening therapy where the assessment indicates that muscle weakness is contributing to loss of function or postural difficulties, and not in the context of any potential benefit for physical activity levels. Therefore this evidence is unlikely to affect the guideline.

The authors noted that other strategies apart from or in addition to resistance training are needed to address the low daily physical activity levels of this population.

New evidence is unlikely to change guideline recommendations.

Physical activity programmes

2-year Evidence Update

No relevant evidence was identified.

4-year surveillance summary

Two reports[10,11] from a multicentre RCT (n=49) examined the effect of a 6-month physical activity stimulation programme on children aged 7–13 years with spastic cerebral palsy, able to walk with and without walking aids (GMFCS level I–III). The physical activity stimulation programme involved counselling through motivational interviewing, home-based physiotherapy, and 4 months of fitness training. The control group continued their usual physiotherapy. Allocation was concealed, assessments were blinded and analysis was intention-to-treat. Assessments were performed at baseline, 4 months, 6 months and 12 months

The first report[10] demonstrated no significant effects of the intervention on primary outcomes (walking activity assessed by activity monitor, and parent-reported physical activity) or secondary outcomes (mobility capacity measured by GMFM-66, walking capacity and functional strength, fitness, self-reported fatigue, and attitude towards sport) at any assessment time. The authors noted positive trends for parent-reported time at moderate-to-vigorous intensity and GMFM-66 at 6 months, but not at 12 months. They also noted a trend for a small, but clinically irrelevant,

improvement in children's attitudes towards the disadvantages of sports at 6 months, and towards the advantages of sports at 12 months.

The second report[11] showed that the intervention resulted in a significant positive effect on social participation in domestic life at 12 months but not at 6 months. No significant effects were found for social participation in recreation and leisure, self-perception at 6 months and 12 months or for quality of life at 12 months.

Three reports[12-14] from a multicentre RCT (n=57) in the Netherlands examined the effect of a 6-month lifestyle intervention on adolescents and young adults aged 16–25 years with unilateral or bilateral spastic cerebral palsy (GMFCS level I–IV). The lifestyle intervention consisted of physical fitness training combined with counselling sessions focused on physical behaviour and sports participation. Analysis was intention to treat.

The first report[12] showed that the lifestyle intervention did not affect physical activity (measured using ambulatory activity monitors) either during the intervention period or at follow-up. Self-reported physical activity (using the Physical Activity Scale for Individuals with Physical Disabilities) was significantly positively affected during the intervention period but the effect was not present at follow-up.

The second report[13] showed that the lifestyle intervention was effective in significantly decreasing fatigue severity during the intervention, and in significantly increasing health-related quality of life with respect to bodily pain and mental health during follow-up. Furthermore, the domain participation and involvement of the social support significantly increased during both the intervention and follow-up period. Physical behaviour or physical fitness explained the observed effects for 22.6%, 9.7% and 28.1% of improvements on fatigue, bodily pain and mental health respectively, but had little effect on social support (2.6%).

The third report[14] was a cost utility analysis. Quality of life (measured by the Short-Form 36 questionnaire) remained stable over time for both groups. No significant differences between groups were found for direct medical costs or productivity costs (collected using standardised questionnaires). A cost-utility ratio of −€23,664 per QALY (derived from the Short-Form 36 using the Short-Form 6D) was found for the lifestyle intervention compared with no treatment.

Topic expert feedback

No topic expert feedback was relevant to this evidence.

Impact statement

The new evidence suggests that programmes to provide and promote physical fitness do not appear to increase objectively measured physical activity, social participation in recreation and leisure, self-perception or quality of life in children, young people or adolescents with spastic cerebral palsy. Some positive effects were seen on other outcomes including social participation in domestic life over the longer term, and fatigue. Effect on quality of life was mixed. The authors of the cost utility report stated that results were exploratory, but indicate that a lifestyle intervention promoting physical activity might be cost-effective or cost-saving compared with offering no intervention to improve physical behaviour and fitness. However, the authors further stated that the large range of uncertainty for the cost-utility ratio should be taken into account and the results interpreted with caution.

The lack of evidence of benefits of these programmes is unlikely to impact CG145, which currently recommends only physical therapy and not physical fitness training. Further research may be needed to draw out the effective components of fitness programmes and their specific effect on different outcomes.

New evidence is unlikely to change guideline recommendations.

Individually defined, targeted physical therapy versus a general programme

2-year Evidence Update

No relevant evidence was identified.

4-year surveillance summary

A pilot single-blind crossover RCT[15] (n=10) evaluated a 10-week individually defined, targeted physical therapy approach versus general physical therapy in children aged 4–

9 years with bilateral spastic cerebral palsy. No significant changes were observed for gross motor function on the GMFM-88. Individual therapy significantly increased step- and stride-length. Change in step-length was significantly higher after the individual programme. Significant within-group effects were found for the pelvis in transversal plane after the individual programme and in coronal plane after the general programme. Significant between-programme differences were found for changes in the knee in sagittal plane, in favour of individual therapy. The median difference in z-score for gait parameters was higher after the individual than the general programme (significance not stated in the abstract). Functional goal attainment was also higher after the individual than the general programme (significance not stated in the abstract).

An evaluator-blinded RCT[16] (n=40) evaluated therapeutic effects and prognostic factors for individualised versus general physical therapy programmes in ambulant children (mean age 6.1 years) with bilateral spastic cerebral palsy. For the primary outcomes, there were higher, but non-significant, changes in Goal Attainment Scale (GAS), and z-score for gait parameters, following the individual versus the general programme. For secondary outcomes, significant time-effects could be found on the GAS and the GMFM-88 total score. Age was identified as a predictor for GAS and GMFM-88 improvement.

Topic expert feedback

No topic expert feedback was relevant to this evidence.

Impact statement

The smaller trial suggested a slightly favourable effect towards the individual physical therapy programme, but the authors stated that to detect clinically significant changes, future studies would need a minimal sample size of 72 to 90 participants. The authors of the larger trial stated that the favourable outcome after the individual programme was not significant and therefore only a trend, and needs to be confirmed in larger groups and with programmes of longer duration. This evidence is unlikely to impact CG145 which already recommends offering a physical therapy programme tailored to the child or young person's individual needs and aimed at specific goals.

New evidence is unlikely to change guideline recommendations.

Computer-game assisted training

2-year Evidence Update

No relevant evidence was identified.

4-year surveillance summary

An assessor-blinded RCT[17] (n=62) compared 6-weeks upper limb training using Wii Sports Resort plus usual therapy with usual therapy alone in children aged 6–13 years with hemiplegic cerebral palsy. There was no significant difference between groups for grip strength at 6 or 12 weeks, or carers' perception of hand function at 6 weeks (though perceived hand function was significantly better in the Wii training group at 12 weeks). There was no difference between groups in coordination or actual hand function at 6 or 12 weeks.

Topic expert feedback

No topic expert feedback was relevant to this evidence.

Impact statement

The new evidence suggests that Wii training does not improve coordination, strength, or hand function. This is unlikely to affect CG145 which does not specifically recommend computer-game assisted training.

New evidence is unlikely to change guideline recommendations.

Orthoses

145 – 03 What is the effectiveness of orthotic interventions (for example, ankle-foot orthoses, knee splints, and upper limb orthoses) as compared to no orthoses to optimise movement and function, to prevent or treat contractures in children with spasticity and with or without other motor disorders caused by a non-progressive brain disorder?

Recommendations derived from this question

General principles

1.3.1 Consider orthoses for children and young people with spasticity based on their individual needs and aimed at specific goals, such as:

- improving posture
- improving upper limb function
- improving walking efficiency
- preventing or slowing development of contractures
- preventing or slowing hip migration
- relieving discomfort or pain
- preventing or treating tissue injury, for example by relieving pressure points.

1.3.2 When considering an orthosis, discuss with the child or young person and their parents or carers the balance of possible benefits against risks. For example, discuss its cosmetic appearance, the possibility of discomfort or pressure sores or of muscle wasting through lack of muscle use.

1.3.3 Assess whether an orthosis might:

- cause difficulties with self-care or care by others
- cause difficulties in relation to hygiene
- be unacceptable to the child or young person because of its appearance.

1.3.4 Ensure that orthoses are appropriately designed for the individual child or young person and are sized and fitted correctly. If necessary seek expert advice from an orthotist within the network team.

1.3.5 Be aware when considering a rigid orthosis that it may cause discomfort or pressure injuries in a child or young person with marked dyskinesia. They should be monitored closely to ensure that the orthosis is not causing such difficulties.

1.3.6 The network of care should have a pathway that aims to minimise delay in:

- supplying an orthosis once measurements for fit have been performed and
- repairing a damaged orthosis.

1.3.7 Inform children and young people who are about to start using an orthosis, and their parents or carers:

- how to apply and wear it
- when to wear it and for how long:
- 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
- an orthosis designed to support a specific function should be worn only when needed
- when and where to seek advice.

1.3.8 Advise children and young people and their parents or carers that they may remove an orthosis if it is causing pain that is not relieved despite their repositioning the limb in the orthosis or adjusting the strapping.

Specific uses

1.3.9 Consider the following orthoses for children and young people with upper limb spasticity:

- elbow gaiters to maintain extension and improve function
- rigid wrist orthoses to prevent contractures and limit wrist and hand flexion deformity
- dynamic orthoses to improve hand function (for example, a non-rigid thumb abduction splint allowing some movement for a child or young person with a 'thumb in palm' deformity).

1.3.10 Consider 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.

1.3.11 Be aware that in children and young people with secondary complications of spasticity, for example contractures and abnormal torsion, ankle–foot orthoses may not be beneficial.

1.3.12 For children and young people with equinus deformities that impair their gait consider:

- a solid ankle–foot orthosis if they have poor control of knee or hip extension
- a hinged ankle–foot orthosis if they have good control of knee or hip extension.

1.3.13 Consider ground reaction force ankle–foot orthoses to assist with walking if the child or young person has a crouch gait and good passive range of movement at the hip and knee.

1.3.14 Consider body trunk orthoses for children and young people with co-existing scoliosis or kyphosis if this will help with sitting.

1.3.15 Consider the overnight use of orthoses to:

- improve posture
- prevent or delay hip migration
- prevent or delay contractures.

1.3.16 Consider the overnight use of orthoses for muscles that control two joints. Immobilising the two adjacent joints provides better stretch and night-time use avoids causing functional difficulties.

1.3.17 If an orthosis is used overnight, check that it:

- is acceptable to the child or young person and does not cause injury
- does not disturb sleep.

Continuing assessment

1.3.18 The network team should review the use of orthoses at every contact with the child or young person. Ensure that the orthosis:

- is still acceptable to the child or young person and their parents or carers
- remains appropriate to treatment goals
- is being used as advised
- remains well fitting and in good repair
- is not causing adverse effects such as discomfort, pain, sleep disturbance, injury or excessive muscle wasting.

Surveillance decision

This review question should not be updated.

(Knee)–ankle–foot orthoses

2-year Evidence Update

An RCT[18] (n=112) compared day-and-night wear of plastic, custom-made, hinged ankle–foot orthoses with day wear only (worn 6–12 hours) in ambulatory children aged 1–4 years with diplegic cerebral palsy (GMFCS levels I and II). Both groups received conventional physiotherapy 5 times a week for the 8-week study period. In both groups, the primary outcome of ankle dorsiflexion had significantly improved at the end of the 8-week study period, but the between-group comparison was not significant. Both groups also showed significant improvements in the other primary outcome of gross motor function (dimensions D and E of the GMFM), with a significantly greater improvement in the day group than the day–night group.

4-year surveillance summary

A pilot crossover RCT[19] (n=11) examined ankle–foot orthoses in children (mean age=4.3 years) with bilateral cerebral palsy. Participants were randomised to wearing or not wearing the orthosis for 2 weeks and then crossed over. Data were collected via an ankle accelerometer. No significant group difference was found in average total daily step count between treatment conditions. When wearing the orthosis, 2 participants (18%) increased total steps/day; 4 (36%) increased walking time; 2 (18%) had more strides at a rate of more than 30 strides/min; and 2 (18%) reached higher peak intensity.

A multicentre RCT[20] (n=28) examined a knee–ankle–foot orthosis (equipped with an Ultraflex ankle power unit) worn for at least 6 hours every other night for 1 year to prevent equinus in children aged 4–16 years with spastic cerebral palsy who were able to walk. Outcomes were measured at baseline and at 3, 6, 9 and 12 months. No significant difference between experimental and control (no orthosis) groups was found in the primary outcome of decrease in ankle-foot dorsiflexion range of motion. Secondary outcome measures (ankle-foot and knee angle in gait and gross motor function) were also not significantly different between groups. The orthosis was only worn for a mean of 3.2 hours per prescribed night due to discomfort.

A double-blind RCT[21] (n=134) compared laser scanning and traditional plaster casting for the construction of ankle–foot orthoses. The time spent in the rectification and moulding of scanned orthoses was around 50% less than for cast orthoses. A non-significant increase of 9 days was seen in the time to delivery to the patient for laser scanning with computer-aided design and computer-aided manufacturing. There was a higher incidence of problems with the scan-based orthoses at delivery of the device, but no difference in how long the orthoses lasted (significance not stated in the abstract). Costs associated with laser scanning were not significantly different from traditional methods of orthosis manufacture.

Topic expert feedback

No topic expert feedback was relevant to this evidence.

Impact statement

The 2-year Evidence Update found that in young ambulatory children with cerebral palsy, wearing ankle–foot orthoses day and night appeared to have no greater effect on ankle range of motion than day wear only. Day and night wear appeared 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), the Evidence Update deemed it was unlikely to have an impact on NICE CG145.

Evidence from 4-year surveillance suggested that ankle–foot orthoses did not consistently enhance walking activity levels or intensity. NICE CG145 recommends ankle–foot orthoses, however the trial was small and the authors noted that larger studies are warranted to confirm the conclusions, therefore this evidence is unlikely to impact CG145.

Further evidence from 4-year surveillance found that knee–ankle–foot orthoses with dynamic ankle and fixed knee do not appear to reduce ankle-foot dorsiflexion range of motion in children with spastic cerebral palsy. This is unlikely to impact CG145 which does not recommend knee-ankle-foot orthoses.

Additionally, the orthosis in the study was only worn for half the recommended time due to discomfort. This reinforces the need for the recommendation in CG145 that if an orthosis is used overnight, it should be checked that it is acceptable to the child or young person and does not cause injury, and does not disturb sleep.

The 4-year surveillance also found evidence that laser scan-based ankle–foot orthosis manufacture did not appear to improve either the quality of the final product or the time to delivery compared with conventional casting.

This evidence is unlikely to affect CG145 which does not recommend specific orthosis manufacture techniques, only that it should be ensured that orthoses are appropriately designed for the individual child or young person and are sized and fitted correctly. It further recommends that the network of care should have a pathway that aims to minimise delay in supplying an orthosis once measurements for fit have been performed.

New evidence is unlikely to change guideline recommendations.

Suit therapy

2-year Evidence Update

No relevant evidence was identified.

4-year surveillance summary

A systematic review and meta-analysis[22] of 4 studies examined 'suit therapy' (details not reported in abstract) for children and adolescents with cerebral palsy. Small, significant pooled effect sizes were found for gross motor function at post-treatment and follow-up. Limitations of the review were noted to be the small number of studies, the variability between them, and the low sample size.

Topic expert feedback

No topic expert feedback was relevant to this evidence.

Impact statement

The authors concluded that to weigh benefits against harms, higher quality evidence is needed on the effect of suit therapy on gross motor function in children and adolescents with cerebral palsy. The limitations of the evidence mean it is unlikely to impact CG145, which does not recommend suit therapy.

New evidence is unlikely to change guideline recommendations.

Oral drugs

145 – 04 What is the effectiveness of oral medications including baclofen, benzodiazepines (diazepam, nitrazepam, clonazepam), tizanidine, dantrolene, clonidine, trihexyphenidyl, tetrabenazine and levodopa in the treatment of spasticity and other motor disorders (dystonia, muscle weakness and choreoathetosis) caused by a non-progressive brain disorder in children and young people?

Recommendations derived from this question

1.4.1 Consider oral diazepam in children and young people if spasticity is contributing to one or more of the following:

- discomfort or pain
- muscle spasms (for example, night-time muscle spasms)
- functional disability.

Diazepam is particularly useful if a rapid effect is desirable (for example, in a pain crisis).

1.4.2 Consider oral baclofen if spasticity is contributing to one or more of the following:

- discomfort or pain
- muscle spasms (for example, night-time muscle spasms)
- functional disability.

Baclofen is particularly useful if a sustained long-term effect is desired (for example, to relieve continuous discomfort or to improve motor function).

1.4.3 If oral diazepam is initially used because of its rapid onset of action, consider changing to oral baclofen if long-term treatment is indicated.

1.4.4 Give oral diazepam treatment as a bedtime dose. If the response is unsatisfactory consider:

- increasing the dose or
- adding a daytime dose.

1.4.5 Start oral baclofen treatment with a low dose and increase the dose stepwise over about 4 weeks to achieve the optimum therapeutic effect.

1.4.6 Continue using oral diazepam or oral baclofen if they have a clinical benefit and are well tolerated, but think about stopping the treatment whenever the child or young person's management programme is reviewed and at least every 6 months.

1.4.7 If adverse effects (such as drowsiness) occur with oral diazepam or oral baclofen, think about reducing the dose or stopping treatment.

1.4.8 If the response to oral diazepam and oral baclofen used individually for 4–6 weeks is unsatisfactory, consider a trial of combined treatment using both drugs.

1.4.9 If a child or young person has been receiving oral diazepam and/or baclofen for several weeks, ensure that when stopping these drugs the dose is reduced in stages to avoid withdrawal symptoms.

1.4.10 In children and young people with spasticity in whom dystonia is considered to contribute significantly to problems with posture, function and pain, consider a trial of oral drug treatment, for example with trihexyphenidyl[a], levodopa[b] or baclofen[c].

a At the time of publication (July 2012), trihexyphenidyl did not have UK marketing authorisation for use in the treatment of dystonia associated with spasticity, and its use is not recommended in children. However, it is used in the UK for the treatment of dystonia in children and young people with spasticity. Informed consent should be obtained and documented.

b At the time of publication (July 2012), levodopa (which is always marketed in combination with an extra-cerebral dopa-decarboxylase inhibitor) did not have UK marketing authorisation for use in the treatment of dystonia associated with spasticity, and its use is not recommended in children or young people. However, it is used in the UK for the treatment of dystonia in children and young people with spasticity. Informed consent should be obtained and documented.

c At the time of publication (July 2012), baclofen did not have UK marketing authorisation for use in the treatment of dystonia associated with spasticity. However, it is used in the UK for the treatment of dystonia in children and young people with spasticity. Informed consent should be obtained and documented.

Surveillance decision

This review question should not be updated.

Tizanidine

2-year Evidence Update

An RCT[23] (n=60) compared tizanidine (2 mg/day for children <7 years and 4 mg/day for children >7 years) with placebo in children aged 2–14 years with hemiplegic cerebral palsy. At the end of the 2-week treatment period, significantly more children who received tizanidine had an improvement in the primary outcome of spastic hypertonia (Modified Ashworth Scale) on the affected side, compared with placebo. In addition, a significantly 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. No serious adverse effects were reported.

4-year surveillance summary

No relevant evidence was identified.

Topic expert feedback

No topic expert feedback was relevant to this evidence.

Impact statement

The 2-year Evidence Update found 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. However, the shortcomings of this study (noted by the Evidence Update as: lack of information on randomisation, allocation concealment and blinding; relatively small sample size and short follow-up; functional abilities not well described; degree of change in Modified Ashworth Scale not reported; pain assessment not well described; side effects not listed) 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. The Evidence Update stated that 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.

New evidence is unlikely to change guideline recommendations.

Levodopa

2-year Evidence Update

No relevant evidence was identified.

4-year surveillance summary

A double-blind, crossover RCT[24] (n=9) compared the effect of levodopa with placebo on upper limb function in young people (mean age 16.8 years) with quadriplegic cerebral palsy and upper limb dystonia. Function was assessed before and after 2 weeks of treatment using box-and-blocks, 9-hole pegs, dynamometer recordings, and Quality of Upper Extremity Skills Test. No benefits for upper limb functional performance were found following levodopa (mean 6.65 +/- 1.66 mg/kg/day) compared to placebo. No side effects were reported.

Topic expert feedback

No topic expert feedback was relevant to this evidence.

Impact statement

No evidence was identified for levodopa during the development of CG145. The full guideline notes that 'Levodopa is used in conditions where the production of dopamine by the brain is insufficient. The Guideline Committee recognised that it is highly effective in treating dopa-responsive dystonia, a genetic condition. The committee concluded that it was reasonable to expect that it might also reduce dystonia in children and young people with spasticity.' CG145 therefore recommends that in children and young people with spasticity in whom dystonia is considered to contribute significantly to problems with posture, function and pain, a trial of oral drug treatment, for example with trihexyphenidyl, levodopa or baclofen, should be considered.

The new evidence suggests that levodopa appears to be of no benefit to upper limb function in young people with quadriplegic cerebral palsy and upper limb dystonia. However, this evidence is from a single small trial and an impact on CG145 is unlikely. Further evidence is needed to examine levodopa in children and young people with cerebral palsy and dystonia.

New evidence is unlikely to change guideline recommendations.

Botulinum toxin type A

145 – 05 What is the effectiveness of the long-term use of intramuscular botulinum toxin A or B in combination with other interventions (physiotherapy/occupational therapy/orthoses) as compared to other interventions at reducing spasticity, maintaining motor function and preventing secondary complications in children with spasticity and with or without other motor disorders (dystonia, muscle weakness and choreoathetosis) caused by a non-progressive brain disorder?

Recommendations derived from this question

General principles

1.5.1 Consider botulinum toxin type A[a] treatment in children and young people in whom focal spasticity of the upper limb is:

- impeding fine motor function
- compromising care and hygiene
- causing pain
- impeding tolerance of other treatments, such as orthoses
- causing cosmetic concerns to the child or young person.

1.5.2 Consider botulinum toxin type A[a] treatment where focal spasticity of the lower limb is:

- impeding gross motor function
- compromising care and hygiene
- causing pain
- disturbing sleep
- impeding tolerance of other treatments, such as orthoses and use of equipment to support posture
- causing cosmetic concerns to the child or young person.

1.5.3 Consider botulinum toxin type A[a] treatment after an acquired non-progressive brain injury if rapid-onset spasticity is causing postural or functional difficulties.

1.5.4 Consider a trial of botulinum toxin type A[b] treatment in children and young people with spasticity in whom focal dystonia is causing serious problems, such as postural or functional difficulties or pain.

1.5.5 Do not offer botulinum toxin type A treatment if the child or young person:

- has severe muscle weakness
- had a previous adverse reaction or allergy to botulinum toxin type A
- is receiving aminoglycoside treatment.

1.5.6 Be cautious when considering botulinum toxin type A treatment if:

- the child or young person has any of the following:
  - a bleeding disorder, for example due to anti-coagulant therapy
  - generalised spasticity
  - fixed muscle contractures
  - marked bony deformity **or**
- there are concerns about the child or young person's likelihood of engaging with the post-treatment adapted physical therapy programme (see recommendation 1.2.15).

1.5.7 When considering botulinum toxin type A treatment, perform a careful assessment of muscle tone, range of movement and motor function to:

- inform the decision as to whether the treatment is appropriate
- provide a baseline against which the response to treatment can be measured.

A physiotherapist or an occupational therapist should be involved in the assessment.

1.5.8 When considering botulinum toxin type A treatment, give the child or young person and their parents or carers information about:

- the possible benefits and the likelihood of achieving the treatment goals
- what the treatment entails, including:
  - the need for assessments before and after the treatment
  - the need to inject the drug into the affected muscles
  - the possible need for repeat injections
  - the benefits, where necessary, of analgesia, sedation or general anaesthesia
  - the need to use serial casting or an orthosis after the treatment in some cases
- possible important adverse effects (see also recommendation 1.5.10).

1.5.9 Botulinum toxin type A treatment (including assessment and administration) should be provided by healthcare professionals within the network team who have expertise in child neurology and musculoskeletal anatomy.

Delivering treatment

1.5.10 Before starting treatment with botulinum toxin type A, tell children and young people and their parents or carers:

- to be aware of the following rare but serious complications of botulinum toxin type A treatment:
  - swallowing difficulties
  - breathing difficulties
- how to recognise signs suggesting these complications are present
- that these complications may occur at any time during the first week after the treatment and
- that if these complications occur the child or young person should return to hospital immediately.

1.5.11 To avoid distress to the child or young person undergoing treatment with botulinum toxin type A, think about the need for:

- topical or systemic analgesia or anaesthesia
- sedation (see Sedation in children and young people, NICE clinical guideline 112).

1.5.12 Consider ultrasound or electrical muscle stimulation to guide the injection of botulinum toxin type A.

1.5.13 Consider injecting botulinum toxin type A into more than one muscle if this is appropriate to the treatment goal, but ensure that maximum dosages are not exceeded.

1.5.14 After treatment with botulinum toxin type A, consider an orthosis to:

- enhance stretching of the temporarily weakened muscle **and**
- enable the child or young person to practice functional skills.

1.5.15 If an orthosis is indicated after botulinum toxin type A, but limited passive range of movement would make this difficult, consider first using serial casting to stretch the muscle. To improve the child or young person's ability to tolerate the cast, and to improve muscle stretching, delay casting until 2–4 weeks after the botulinum toxin type A treatment.

1.5.16 Ensure that children and young people who receive treatment with botulinum toxin type A are offered timely access to orthotic services.

Continuing assessment

1.5.17 Perform an assessment of muscle tone, range of movement and motor function:

- 6–12 weeks after injections to assess the response
- 12–26 weeks after injections to inform decisions about further injections.

  These assessments should preferably be performed by the same healthcare professionals who undertook the baseline assessment.

1.5.18 Consider repeat injections of botulinum toxin type A if:

- the response in relation to the child or young person's treatment goal was satisfactory, and the treatment effect has worn off
- new goals amenable to this treatment are identified.

a At the time of publication (July 2012), 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.

b At the time of publication (July 2012), botulinum toxin type A did not have UK marketing authorisation for use in the treatment of focal dystonia associated with spasticity. However, it is used in the UK for the treatment of dystonia in children and young people with spasticity. Informed consent should be obtained and documented.

Surveillance decision

This review question should not be updated.

Single dose of Botulinum toxin type A

2-year Evidence Update

No relevant evidence was identified.

4-year surveillance summary

A systematic review and meta-analysis[25] of 32 RCTs examined a single dose of botulinum toxin type A for improving ease of care in the upper and lower limbs in adults with difficulty in caring for the upper/lower limb resulting from spasticity of any origin. Meta-analysis was carried out on 11 upper limb and 3 lower limb studies. Evidence quality for the upper limb was moderate. A significant result for botulinum toxin type A was found at 4 to 12 weeks for the upper limb. The effects were significantly maintained for up to 6 months. Evidence quality was very low for the lower limb. Meta-analysis was only possible for global assessment of benefit. No significant effect was found.

Topic expert feedback

Topic experts noted that there are quite a few new papers about the use of botulinum toxin in managing spasticity in children.

Impact statement

The new evidence suggests that botulinum toxin type A can improve ease of care in the upper limb of adults for up to 6 months. This is consistent with the recommendation in CG145 that botulinum toxin type A treatment should be considered in children and young people in whom focal spasticity of the upper limb is (among other issues) compromising care and hygiene. However, the generalisability of this evidence to CG145 is unclear because the meta-analysis did not include any children.

New evidence is unlikely to change guideline recommendations.

Botulinum toxin type A: 10 versus 15 U/kg/leg

2-year Evidence Update

No relevant evidence was identified.

4-year surveillance summary

An RCT[26] (n=241) examined botulinum toxin type A (abobotulinumtoxinA) for dynamic equinus foot deformity in children with cerebral

palsy. Patients were randomised (1:1:1) to botulinum toxin type A 10 U/kg/leg, 15 U/kg/leg, or placebo injections into the gastrocnemius-soleus complex (1 or both legs injected). In the primary hierarchical analysis, demonstration of benefit for each dose required superiority to placebo on the primary (change in spasticity on Modified Ashworth Scale from baseline to week 4) and first key secondary (Physician's Global Assessment at week 4) end points. At week 4, Modified Ashworth Scale scores significantly improved with botulinum toxin type A versus placebo (a numerically greater difference was seen with 15 U/kg/leg than 10 U/kg/leg, but significance of between-group difference not reported in abstract). The Physician's Global Assessment treatment differences versus placebo were also significant (a numerically greater difference for this outcome was seen with 10 U/kg/leg than 15 U/kg/leg, but again significance of between-group difference was not reported in the abstract). The most common treatment-related adverse event was muscular weakness (10 U/Kg/leg=2; placebo=1).

Topic expert feedback

Topic experts noted that there are quite a few new papers about the use of botulinum toxin in managing spasticity in children.

Impact statement

The new evidence suggests that botulinum toxin type A can improve spasticity in children with dynamic equinus foot deformity resulting in an improved overall clinical impression with few treatment-related adverse events. CG145 does not discuss botulinum toxin dose, and is unlikely to be affected by this evidence. The evidence is consistent with the recommendation in CG145 to consider botulinum toxin type A treatment where focal spasticity (dynamic equinus foot deformity being an example) of the lower limb is: impeding gross motor function; compromising care and hygiene; causing pain; disturbing sleep; impeding tolerance of other treatments, such as orthoses and use of equipment to support posture; causing cosmetic concerns to the child or young person.

New evidence is unlikely to change guideline recommendations.

Repeat botulinum toxin type A

2-year Evidence Update

No relevant evidence was identified.

4-year surveillance summary

A systematic review[27] of 13 studies (n=893) examined the effects of repeat botulinum toxin type A injections in children with spastic cerebral palsy. The critical review form produced by McMaster University was used to determine study methodological quality, then levels of evidence were confirmed from Sackett. The studies were also evaluated using the International Classification of Function, Disability and Health - Children and Youth Version. The evidence level was II in 4 studies, III in 4 studies, and IV in 5 studies. The McMaster review form score was 14 in 2 studies, 13 in 4 studies, and 12 in 7 studies. The results showed that repeat botulinum toxin type A may be a safe and an effective approach. The first 2 injections/1 repeat especially relieve spasticity and improve fine and gross motor activities (significance not reported in abstract).

Topic expert feedback

Topic experts noted that there are quite a few new papers about the use of botulinum toxin in managing spasticity in children.

Impact statement

The new evidence suggests that repeat botulinum toxin type A may be safe and effective to relieve spasticity and improve fine and gross motor activities. Within the limited data reported, this evidence appears consistent with the recommendation in CG145 to consider repeat injections of botulinum toxin type A if: the response in relation to the child or young person's treatment goal was satisfactory, and the treatment effect has worn off; new goals amenable to this treatment are identified.

New evidence is unlikely to change guideline recommendations.

Botulinum toxin type A injection at different muscle sites

2-year Evidence Update

No relevant evidence was identified.

4-year surveillance summary

An RCT[28] (n=34 gracilis muscles, in 27 children) examined motor endplate-targeted botulinum toxin type A injections at different sites of the gracilis muscle in children (mean age 8.6 years) with unilateral and bilateral spastic cerebral palsy (GMFCS levels I–IV). In one group, botulinum toxin type A was injected proximally (at a site 25% of the distance from the pubic tubercle and the medial epicondyle) and in the other group it was injected at the motor endplate zones (half of the dose was administered at 30% of this distance and half at 60%). For the primary outcome, spasticity decreased significantly more in motor endplate-targeted muscles than in proximally injected muscles, as demonstrated by a larger reduction in average velocity-dependent change in average root mean square electromyography values. However, this difference was not found for the secondary outcome of spasticity measured on the Modified Ashworth Scale and Modified Tardieu Scale.

Topic expert feedback

Topic experts noted that there are quite a few new papers about the use of botulinum toxin in managing spasticity in children.

Impact statement

The new evidence suggests that botulinum toxin type A injection of the gracilis muscle at sites with a high concentration of motor endplates is effective at reducing spasticity. The authors noted that in the case of long muscles, such as the gracilis, the injection site is important. However, the authors further noted that these preliminary findings should be confirmed by larger studies. This evidence is therefore unlikely to affect CG145, which does not currently make any specific recommendations on injection sites.

New evidence is unlikely to change guideline recommendations.

Botulinum toxin type A plus physical therapy versus physical therapy alone

2-year Evidence Update

No relevant evidence was identified.

4-year surveillance summary

A double-blind RCT[29] (n=41) examined botulinum toxin type A versus sham, combined with 'therapy' (undefined), for nonambulatory children aged 2.3–16 years with cerebral palsy (GMFCS level IV–V). Adverse events were collected at 2, 4, and 16 weeks by a physician masked to group allocation. For the primary outcome, there were significant between group differences favouring botulinum toxin type A for Canadian Occupational Performance Measure–performance at 4 weeks and for Canadian Occupational Performance Measure–satisfaction. These significant effects were retained at 16 weeks for the satisfaction component. There were significantly more mild adverse events at 4 weeks with botulinum toxin type A, however, there were no significant between-group differences in the reporting of moderate and serious adverse events.

An RCT[30] (n=27) examined upper limb botulinum toxin versus sham, combined with physiotherapy/orthoses, in children with spastic hemiplegic cerebral palsy. Every patient was given a specific physiotherapeutic treatment, consisting of individualised goal directed exercises, task oriented activities, daily stretching manoeuvres, functional and/or static orthoses. For the primary outcome, the botulinum toxin type A group showed a significant increase of Assisting Hand Assessment raw scores at 3 months, compared to controls. Functional goals achievement as measured by Goal Attainment Scaling was also significantly better (although the authors stated only slightly) with botulinum toxin type A. Other measures indicated some improvement in both groups, without significant between group differences. Children with intermediate severity of hand function on the House scale for upper limb impairment seemed to benefit more from botulinum toxin type A (data not reported in abstract).

An evaluator-blinded RCT[31] (n=20) examined repeated botulinum toxin type A injections combined with occupational therapy, including a splint, compared with occupational therapy alone, on hand function in children with unilateral spastic cerebral palsy (in all

International Classification of Functioning, Disability and Health domains). Interventions were carried out over the course of 1 year. For the primary outcome, a superior effect on the Assisting Hand Assessment was seen in the botulinum toxin type A group at 12 months. Secondary outcomes (range of movement, and Canadian Occupational Performance Measure) improved in both groups (significance not stated in the abstract).

Topic expert feedback

Topic experts noted that there are quite a few new papers about the use of botulinum toxin in managing spasticity in children.

Impact statement

The new evidence suggests that botulinum toxin type A (singly or repeated) combined with physical therapy and/or orthoses appears to improve Canadian Occupational Performance Measure scores (that is, an individual's perceived occupational performance in the areas of self-care, productivity, and leisure) and improve hand function, with no increase in moderate and severe adverse events. However, the studies were small.

The evidence is consistent with the recommendation in CG145 that following treatment with botulinum toxin type A, an adapted physical therapy programme should be provided as an essential component of management, and the further recommendation that after treatment with botulinum toxin type A, an orthosis should be considered.

New evidence is unlikely to change guideline recommendations.

Botulinum toxin type A plus abduction bracing versus standard care

2-year Evidence Update

A long-term follow up of an RCT[32] (n=46) examined 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 RCT 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. Children were aged 1–5 years at enrolment and were at risk of hip displacement, with a hip migration percentage of 10–40%. After the 3-year study period, the rate of hip displacement and surgery was lower in the intervention group than the standard care group, but both groups continued to report hip displacement. The present analysis followed up 46 children.

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 the primary outcomes of hip migration or morphology (mean percentage hip migration 15–16% in both groups, and most children in both groups had 'satisfactory' hip morphology). A similar number of children in both groups needed preventive or reconstructive surgery, or both, during long-term follow-up. 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.

4-year surveillance summary

No relevant evidence was identified.

Topic expert feedback

Topic experts noted that there are quite a few new papers about the use of botulinum toxin in managing spasticity in children.

Impact statement

The 2-year Evidence Update found that early non-operative intervention with botulinum toxin type A injections and abduction bracing in children with cerebral palsy at risk of hip displacement does not appear to improve long-term hip development versus 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 (noted by the Evidence Update to be: lack of outcome measures of function, activity and participation; observational follow-up design at 1 centre; not adjusting for confounding factors; and not possible to distinguish effects of botulinum toxin type A from abduction bracing), and along with the small size of the study, this evidence was deemed unlikely to affect CG145.

New evidence is unlikely to change guideline recommendations.

Safety of botulinum toxin type A

2-year Evidence Update

No relevant evidence was identified.

4-year surveillance summary

An RCT[33] (n=41) examined the safety of botulinum toxin type A in nonambulatory children with cerebral palsy. In cycle 1 of the study, children were randomised to botulinum toxin type A injection or sham. In cycle 2, the botulinum toxin type A group received a second episode of botulinum toxin type and the sham group received their first episode of botulinum toxin type A. A paediatric rehabilitation specialist masked to group allocation graded each adverse event according to system, severity and likelihood of it being related to the intervention. There was no significant difference between the groups for all moderate or serious adverse events in either cycle 1 or cycle 2. In Cycle 2, 1 serious, 3 moderate (single-episode group), and 24 mild (single-episode group n=10; double-episode group n=14) adverse events were probably/definitely related to botulinum toxin type A.

A double-blind RCT[34] (n=35) examined the safety of incobotulinum toxin type A (Xeomin; note – not licensed for children in the UK). The study authors noted that there are only 2 preparations of botulinum toxin type A for which there is published evidence of efficacy in children with cerebral palsy: onabotulinum toxin type A (Botox) and abobotulinum toxin type A (Dysport). This trial examined the safety profile of incobotulinum toxin type A (Xeomin) in children aged 3–18 years with spastic hemiplegic or diplegic cerebral palsy. Children were randomised to injection in gastrocnemius (medialis and lateralis) muscles with 5 units/kg of either incobotulinum toxin type A or onabotulinum toxin type A. Adverse events were recorded at baseline, 48 hours, 10 days and 3 months by caregivers on a checklist that listed both common and uncommon side effects. At least 1 adverse event occurred in 49% of patients within the first 2 days, 46% between 2 and 10 days, and 12% between 10 and 90 days. All reported events were minor; no serious adverse event was recorded. Fatigue was the most frequent complaint. There was no significant difference in frequency and type of events between the 2 groups.

Topic expert feedback

Topic experts noted that there are quite a few new papers about the use of botulinum toxin in managing spasticity in children. They cover some of the topics for which there was little or no evidence – such as different toxin subtypes.

Impact statement

The new evidence suggests that children receiving botulinum toxin type A were at no greater risk of moderate/serious adverse events compared with sham. There also appeared to be no increased risk of moderate/serious adverse events between 1 and 2 episodes of botulinum toxin type A. This evidence is consistent with the recommendation in CG145 to consider botulinum toxin type A, but that before starting treatment with botulinum toxin type A, children and young people and their parents or carers should be told to be aware of rare but serious complications of botulinum toxin type A treatment.

The new evidence additionally suggests that incobotulinum toxin type A and onabotulinum toxin type A share a similar safety profile in the treatment of lower limb spasticity. This evidence is unlikely to affect CG145, which does not specify any particular botulinum toxin type A product. Prescribers should note the following information taken from the introduction, and footnote 6, of the NICE version of the guideline:

‘The guideline will assume that prescribers will use a drug's summary of product characteristics (SPC) to inform decisions made with individual patients. This guideline recommends some drugs for indications for which they do not have a UK marketing authorisation at the date of publication, if there is good evidence to support that use. Where recommendations have been made for the use of drugs outside their licensed indications ('off-label use'), these drugs are marked with a footnote in the recommendations.’

'At the time of publication (July 2012), 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.'

New evidence is unlikely to change guideline recommendations.

Efficacy of injection with techniques to aid placement of botulinum toxin type A; parents and child's experiences of injections

2-year Evidence Update

No relevant evidence was identified.

4-year surveillance summary

No relevant evidence was identified.

Topic expert feedback

Topic experts noted that there are quite a few new papers about the use of botulinum toxin in managing spasticity in children. They cover some of the topics for which there was little or no evidence – such as efficacy of injection with techniques to aid placement of toxin, and parents' and children's experiences of injection. An article was suggested which related to parents' and children's experiences of injection, however this was excluded on the basis of study type.

Impact statement

No evidence was identified therefore no impact on CG145 is expected.

New evidence is unlikely to change guideline recommendations.

Intrathecal baclofen

145 – 06 In children and young people with spasticity due to a non-progressive brain disorder does an intrathecal baclofen test help to identify those likely to benefit from continuous pump administered intrathecal baclofen?

Recommendations derived from this question

General principles

1.6.1 Consider treatment with continuous pump-administered intrathecal baclofen[a] in children and young people with spasticity if, despite the use of non-invasive treatments, spasticity or dystonia are causing difficulties with any of the following:

- pain or muscle spasms
- posture or function
- self-care (or ease of care by parents or carers).

1.6.2 Be aware that children and young people who benefit from continuous pump-administered intrathecal baclofen typically have:

- moderate or severe motor function problems (GMFCS level III, IV or V)
- bilateral spasticity affecting upper and lower limbs.

1.6.3 Be aware of the following contraindications to treatment with continuous pump-administered intrathecal baclofen:

- the child or young person is too small to accommodate an infusion pump
- local or systemic intercurrent infection.

1.6.4 Be aware of the following potential contraindications to treatment with continuous pump-administered intrathecal baclofen:

- co-existing medical conditions (for example, uncontrolled epilepsy or coagulation disorders)
- a previous spinal fusion procedure
- malnutrition, which increases the risk of post-surgical complications (for example, infection or delayed healing)
- respiratory disorders with a risk of respiratory failure.

1.6.5 If continuous pump-administered intrathecal baclofen is indicated in a child or young person with spasticity in whom a spinal fusion procedure is likely to be necessary for scoliosis, implant the infusion pump before performing the spinal fusion.

1.6.6 When considering continuous pump-administered intrathecal baclofen, balance the benefits of reducing spasticity against the risk of doing so because spasticity sometimes supports function (for example, by compensating for muscle weakness). Discuss these possible adverse effects with the child or young person and their parents or carers.

1.6.7 When considering continuous pump-administered intrathecal baclofen, inform children and young people and their parents or carers verbally and in writing (or appropriate formats) about:

- the surgical procedure used to implant the pump
- the need for regular hospital follow-up visits
- the requirements for pump maintenance
- the risks associated with pump implantation, pump-related complications and adverse effects that might be associated with intrathecal baclofen infusion.

Intrathecal baclofen testing

1.6.8 Before making the final decision to implant the intrathecal baclofen pump, perform an intrathecal baclofen test to assess the therapeutic effect and to check for adverse effects.

1.6.9 Before intrathecal baclofen testing, inform children and young people and their parents or carers verbally and in writing (or appropriate formats) about:

- what the test will entail
- adverse effects that might occur with testing
- how the test might help to indicate the response to treatment with continuous pump-administered intrathecal baclofen, including whether:
  - the treatment goals are likely to be achieved
  - adverse effects might occur.

1.6.10 Before performing the intrathecal baclofen test, assess the following where relevant to the treatment goals:

- spasticity
- dystonia
- the presence of pain or muscle spasms
- postural difficulties, including head control
- functional difficulties
- difficulties with self-care (or ease of care by parents or carers).

  If necessary, assess passive range of movement under general anaesthesia.

1.6.11 The test dose or doses of intrathecal baclofen should be administered using a catheter inserted under general anaesthesia.

1.6.12 Assess the response to intrathecal baclofen testing within 3–5 hours of administration. If the child or young person is still sedated from the general anaesthetic at this point, repeat the assessment later when they have recovered.

1.6.13 When deciding whether the response to intrathecal baclofen is satisfactory, assess the following where relevant to the treatment goals:

- reduction in spasticity
- reduction in dystonia
- reduction in pain or muscle spasms
- improved posture, including head control
- improved function
- improved self-care (or ease of care by parents or carers).

1.6.14 Discuss with the child or young person and their parents or carers their views on the response to the intrathecal baclofen test. This should include their assessment of the effect on self-care (or ease of care by parents or carers). Consider using a standardised questionnaire to document their feedback.

1.6.15 Intrathecal baclofen testing should be:

- performed in a specialist neurosurgical centre within the network that has the expertise to carry out the necessary assessments
- undertaken in an inpatient setting to support a reliable process for assessing safety and effectiveness.

1.6.16 Initial and post-test assessments should be performed by the same healthcare professionals in the specialist neurosurgical centre.

a At the time of publication (July 2012), intrathecal baclofen did not have UK marketing authorisation for children younger than 4 years, nor did it have UK marketing authorisation for use in the treatment of dystonia associated with spasticity. Where appropriate, informed consent should be obtained and documented.

Surveillance decision

This review question should not be updated.

Lumbar puncture or other short-term means of delivering intrathecal baclofen

2-year Evidence Update

No relevant evidence was identified.

4-year surveillance summary

A Cochrane review[35] of 6 studies examined intrathecal baclofen for treating spasticity in children with cerebral palsy. The data obtained were unsuitable for meta-analysis so a qualitative summary was done. All studies were found to have high or unclear risk of bias in some aspects of their methodology. Five studies reported data collected in the randomised controlled phase of the study. A sixth study did not report sufficient results to determine the effect of intrathecal baclofen versus placebo. Of these 5 studies, 4 were conducted using lumbar puncture or other short-term means of delivering intrathecal baclofen (that is, a methodology more aligned with an intrathecal baclofen test). These 4 short-term studies demonstrated that intrathecal baclofen therapy reduces spasticity in children with cerebral palsy. However, 2 of these studies utilised inappropriate techniques for statistical analysis of results. One of these studies showed improvement in comfort and ease of care. The authors noted some caution is required in interpreting the findings of the studies in the review due to methodological issues.

Topic expert feedback

Topic experts noted that the original guideline had little evidence on the benefits and cost effectiveness of intrathecal baclofen trials. An article was suggested but was excluded on study type.

Impact statement

The Cochrane authors concluded that there is some limited short-term evidence that

intrathecal baclofen is an effective therapy for reducing spasticity in children with cerebral palsy. The validity of the evidence for the effectiveness of intrathecal baclofen in treating spasticity in children with cerebral palsy from the studies in the review is constrained by the small sample sizes of the studies and methodological issues in some studies. However, these studies were not examined in the context of whether an intrathecal baclofen test can help to identify those likely to go on to benefit from continuous pump administered intrathecal baclofen. Additionally, all 6 of the studies included in the Cochrane review were examined by the Guideline Committee during the development of CG145, of which 3 were included and 3 excluded from the guideline. This evidence is therefore unlikely to affect the recommendation in CG145 that before making the final decision to implant the intrathecal baclofen pump, an intrathecal baclofen test should be performed to assess the therapeutic effect and to check for adverse effects.

New evidence is unlikely to change guideline recommendations.

---

145 – 07 In children and young people with spasticity due to a non-progressive brain disorder what are the benefits and risks of continuous intrathecal baclofen therapy?

Recommendations derived from this question

1.6.17 Before implanting the intrathecal baclofen pump, inform children and young people and their parents or carers, verbally and in writing (or appropriate formats), about:

- safe and effective management of continuous pump-administered intrathecal baclofen
- the effects of intrathecal baclofen, possible adverse effects, and symptoms and signs suggesting the dose is too low or too high
- the potential for pump-related complications
- the danger of stopping the continuous pump-administered intrathecal baclofen infusion suddenly
- the need to attend hospital for follow-up appointments, for example to refill and reprogram the infusion pump
- the importance of seeking advice from a healthcare professional with expertise in intrathecal baclofen before stopping the treatment.

1.6.18 Implant the infusion pump and start treatment with continuous pump-administered intrathecal baclofen within 3 months of a satisfactory response to intrathecal baclofen testing (see recommendation 1.6.13).

1.6.19 Support children and young people receiving treatment with continuous pump-administered intrathecal baclofen and their parents or carers by offering regular follow-up with the network team, and a consistent point of contact with the specialist neurosurgical centre.

1.6.20 Monitor the response to continuous pump-administered intrathecal baclofen. This monitoring should preferably be performed by the healthcare professionals in the regional specialist neurosurgical centre who performed the pre-implantation assessments.

1.6.21 When deciding whether the response to continuous pump-administered intrathecal baclofen is satisfactory, assess the following where relevant to the treatment goals:

- reduction in spasticity
- reduction in dystonia
- reduction in pain or muscle spasms
- improved posture, including head control

- improved function
- improved self-care (or ease of care by parents or carers).

1.6.22 Titrate the dose of intrathecal baclofen after pump implantation, if necessary, to optimise effectiveness.

1.6.23 If treatment with continuous pump-administered intrathecal baclofen does not result in a satisfactory response (see recommendation 1.6.21), check that there are no technical faults in the delivery system and that the catheter is correctly placed to deliver the drug to the intrathecal space. If no such problems are identified, consider reducing the dose gradually to determine whether spasticity and associated symptoms increase.

1.6.24 If continuous pump-administered intrathecal baclofen therapy is unsatisfactory, the specialist neurosurgical centre and other members of the network team should discuss removing the pump and alternative management options with the child or young person and their parents or carers.

1.6.25 As the infusion pump approaches the end of its expected lifespan, consider reducing the dose gradually to enable the child or young person and their parents or carers to decide whether or not to have a new pump implanted..

Surveillance decision

This review question should not be updated.

Continuous intrathecal baclofen therapy

2-year Evidence Update

No relevant evidence was identified.

4-year surveillance summary

A Cochrane review[35] of 6 studies examined intrathecal baclofen for treating spasticity in children with cerebral palsy (see previous commentary above for details). Only 1 of the 6 included studies assessed the effectiveness of implantable intrathecal baclofen pumps, over a period of 6 months. It demonstrated minimal reduction in spasticity with the use of intrathecal baclofen therapy, but did show improvement in comfort and ease of care. It also found a small improvement in gross motor function and also in some domains of health-related quality of life. The authors noted there was a high risk of bias in the methodology of the 1 study of implantable intrathecal baclofen pumps due to the lack of placebo use in the control group and the absence of blinding to the intervention after randomisation for both participants and investigators.

A retrospective cohort study[36] (n=254) examined risk factors for baclofen pump infection in children. Patients who underwent implantation of a programmable pump and intrathecal catheter for baclofen infusion at a single centre between January 2000 and March 2012 were identified. Univariate analysis was performed, and a multivariate logistic regression model was created to identify independent risk factors for infection. The primary endpoint of overall infection rate was 9.8%. Univariate analysis identified young age, shorter height, lower weight, dehiscence, cerebrospinal fluid leak, and number of revisions within 6 months of pump placement as significantly associated with infection. Multivariate analysis identified young age, dehiscence, and number of revisions as independent risk factors for infection. A low BMI and the presence of either a gastrostomy or tracheostomy were not associated with infection.

Topic expert feedback

Topic experts suggested a study of intrathecal baclofen that looked at activities of daily living and patient satisfaction of treatment, which they noted was missing from papers reviewed at the time of the guideline. However this paper was excluded on study type.

Topic experts also noted that there were now more studies on complications and safety of intrathecal baclofen therapy in children (of which 1 has been included in the 4-year surveillance).

Experts further noted that there is now more than one Intrathecal Drug Delivery System on the market in UK.

It was also noted that an MHRA warning was issued in 2013 about implantable drug pumps.

Topic experts additionally noted the need to check costs for intrathecal baclofen.

Impact statement

The authors of the Cochrane review concluded that the effect of intrathecal baclofen on long-term spasticity outcomes is less certain. The validity of the evidence for the effectiveness of intrathecal baclofen in treating spasticity in children with cerebral palsy from the studies in the review is constrained by the small sample sizes of the studies and methodological issues in some studies. There is some evidence that intrathecal baclofen improves ease of care and the comfort and quality of life of the individuals receiving it, but again small sample sizes and methodological issues in the studies mean that these results should be interpreted with caution. The authors stated that further evidence of the effectiveness of intrathecal baclofen for treating spasticity, increasing gross motor function and improving comfort, ease of care and quality of life is needed from other investigators in order to validate these results. The short duration of the controlled studies included in this review did not allow for the exploration of questions regarding whether the subsequent need for orthopaedic surgery in children receiving intrathecal baclofen therapy is altered, or the safety and the economic implications of intrathecal baclofen treatment when long-term therapy is administered via an implanted device. The authors suggested that controlled studies are not the most appropriate study design to address these questions, and cohort studies may be more appropriate. This suggestion is consistent with the priority research recommendation in CG145 'What is the clinical and cost effectiveness of continuous pump-administered intrathecal baclofen compared with usual care in children and young people who are at GMFCS level IV or V?', for which relevant research designs are noted to include RCTs, prospective cohort studies and qualitative studies.

All 6 of the studies included in the Cochrane review were examined by the Guideline Committee during the development of CG145, of which 3 were included and 3 excluded from the guideline. This, along with the limitations of the evidence, means that any impact on the recommendation in CG145 to consider treatment with continuous pump-administered intrathecal baclofen is unlikely.

Additional evidence from the 4-year surveillance found that young age, wound dehiscence, and number of revisions appeared to be independent risk factors for baclofen pump infection. A low BMI and the presence of either a gastrostomy or tracheostomy were not associated with infection and may not be contraindications for this procedure. In its recommendations on 'General principles' for intrathecal baclofen (see previous review question 145–06 for the full list) CG145 already recommends being aware of several contraindications and potential contraindications to treatment with continuous pump-administered intrathecal baclofen:

- the child or young person is too small to accommodate an infusion pump
- local or systemic intercurrent infection
- co-existing medical conditions (for example, uncontrolled epilepsy or coagulation disorders)
- a previous spinal fusion procedure
- malnutrition, which increases the risk of post-surgical complications (for example, infection or delayed healing)
- respiratory disorders with a risk of respiratory failure.

This list broadly caters for the issues raised by the evidence and an impact on CG145 is unlikely.

The MHRA warning was not thought to impact on recommendations.

New evidence is unlikely to change guideline recommendations

Orthopaedic surgery

145 – 08 What is the effectiveness of orthopaedic surgery in preventing or treating musculoskeletal deformity in children with spasticity caused by a non-progressive brain disorder?

Recommendations derived from this question

1.7.1 Consider orthopaedic surgery as an important adjunct to other interventions in the management programme for some children and young people with spasticity. Timely surgery can prevent deterioration and improve function.

1.7.2 An assessment should be performed by an orthopaedic surgeon within the network team if:

- based on clinical findings (see recommendation 1.1.16) or radiological monitoring, there is concern that the hip may be displaced
- based on clinical or radiological findings there is concern about spinal deformity.

1.7.3 Consider an assessment by an orthopaedic surgeon in the network team for children and young people with:

- hip migration greater than 30% or
- hip migration percentage increasing by more than 10 percentage points per year.

1.7.4 Consider an assessment by an orthopaedic surgeon in the network team if any of the following are present:

- limb function is limited (for example, in walking or getting dressed) by unfavourable posture or pain, as a result of muscle shortening, contractures or bony deformities
- contractures of the shoulder, elbow, wrist or hand cause difficulty with skin hygiene
- the cosmetic appearance of the upper limb causes significant concern for the child or young person.

1.7.5 Before undertaking orthopaedic surgery, the network team should discuss and agree with the child or young person and their parents or carers:

- the possible goals of surgery and the likelihood of achieving them
- what the surgery will entail, including any specific risks
- the rehabilitation programme, including:
  - how and where it will be delivered
  - what the components will be, for example a programme of adapted physical therapy, the use of orthoses, oral drugs or botulinum toxin type A.

1.7.6 Orthopaedic surgery should:

- be undertaken by surgeons in the network team who are expert in the concepts and techniques involved in surgery for this group of patients and
- take place in a paediatric setting.

1.7.7 The decision to perform orthopaedic surgery to improve gait should be informed by a thorough pre-operative functional assessment, preferably including gait analysis.

1.7.9 Assess the outcome of orthopaedic surgery undertaken to improve gait 1–2 years later. By then full recovery may be expected and the outcome of the procedure can be more accurately determined.

Surveillance decision

This review question should not be updated.

Femoral derotation osteotomy

2-year Evidence Update

No relevant evidence was identified.

4-year surveillance summary

A systematic review and meta-analysis[37] of 13 cohort studies (5 prospective, 8 retrospective) examined the effect of femoral derotation osteotomy on transverse plane hip and pelvic rotation kinematics in children with spastic cerebral palsy. Meta-analysis showed that femoral derotation osteotomy significantly reduced pelvic retraction by 9.0 degrees and hip internal rotation by 17.6 degrees in participants with unilateral cerebral palsy involvement and hip internal rotation by 14.3 degrees in participants with bilateral cerebral palsy involvement.

Topic expert feedback

No topic expert feedback was relevant to this evidence.

Impact statement

The new evidence found that pelvic symmetry in children with unilateral spastic cerebral palsy appears to be improved by femoral derotation osteotomy. Patients with bilateral involvement do not appear to improve their transverse plane pelvic rotation profiles during gait as a result of femoral derotation osteotomy. CG145 does not specify any particular types of orthopaedic surgery. However, the authors noted that the evidence should be interpreted with caution due to the heterogeneous nature of participants and the methods used in the studies assessed, and is therefore unlikely to affect CG145.

New evidence is unlikely to change guideline recommendations.

Reconstructive surgery for hip displacement

2-year Evidence Update

No relevant evidence was identified.

4-year surveillance summary

A systematic review[38] of 29 studies examined the frequency and risk factors of avascular necrosis following reconstructive surgery for hip displacement in children with cerebral palsy. The frequency of avascular necrosis ranged from 0–46% with an overall rate across studies of 7.5%. Presence of avascular necrosis was the primary outcome in 2 studies. The frequency of avascular necrosis in these studies was significantly higher than other studies at 37% and 46%. No significant associations were found between age at surgery, severity of hip subluxation, length of follow-up, or type of surgery (combined varus derotation osteotomy and pelvic osteotomy versus varus derotation osteotomy alone), and the rate of avascular necrosis. The majority of studies did not comment on methods used for determining diagnosis or severity of avascular necrosis and clinical significance was not well documented.

Topic expert feedback

No topic expert feedback was relevant to this evidence.

Impact statement

The new evidence found that children with cerebral palsy undergoing reconstructive hip surgery may be at risk of developing avascular necrosis. No significant risk factors were identified. The authors noted that the incidence of avascular necrosis was higher in studies in which avascular necrosis was a primary outcome, which may suggest that the true frequency of avascular necrosis may be higher than is currently understood. This evidence is consistent with the recommendation in CG145 that before undertaking orthopaedic surgery, the network team should discuss and agree with the child or young person and their parents or carers what the surgery will entail, including any specific risks.

New evidence is unlikely to change guideline recommendations.

145 – 09 What is the effectiveness of single event multilevel orthopaedic surgery in managing musculoskeletal deformity in children with spasticity caused by a non-progressive brain disorder?

Recommendations derived from this question

1.7.8 If a child or young person will need several surgical procedures at different anatomical sites to improve their gait, perform them together if possible (single-event multilevel surgery), rather than individually over a period of time.

Surveillance decision

This review question should not be updated.

Single event multilevel muscle tendon surgery, osteotomies, and dorsal rhizotomy

2-year Evidence Update

No relevant evidence was identified.

4-year surveillance summary

A retrospective cohort study[39] (n=94) compared effects of single-event multilevel muscle tendon surgery, osteotomies, and dorsal rhizotomy for children aged 4–18 years with cerebral palsy (GMFCS classification I–III). No statistically significant differences in change scores were found between groups in the GMFM, velocity, or stride length measures after the observation period. The selective dorsal rhizotomy group had greater improvements in knee extension when compared with the nonsurgical group and greater hip and knee total range of motion during the gait cycle when compared with nonsurgical group and the muscle-tendon surgery and osteotomy cohorts (significance not stated). Lastly, the muscle-tendon surgery group had greater improvements in total knee range of motion compared with the nonsurgical group (significance not stated in the abstract).

Topic expert feedback

The topic experts stated that the subject of the above study[39] is a comparison that the Guideline Committee was interested in.

The topic experts also drew attention to the NHS England project of Commissioning through Evaluation of selective dorsal rhizotomy, which has affected availability of NHS funding for the procedure. They stated that there was unlikely to be a decision until 2017/2018.

Impact statement

The new evidence suggests that patients who undergo selective dorsal rhizotomy and, to a lesser extent, muscle tendon procedures appear to demonstrate greater improvements in kinematic gait variables compared with nonsurgical interventions in patients with spasticity resulting from cerebral palsy. However, in the full version of the guideline it was noted by the Guideline Committee that many research studies often present detailed gait outcomes, but the Committee preferred to focus on velocity and distance as these are important to patients. Therefore the lack of difference between groups for more preferred outcomes means this evidence is unlikely to impact CG145.

It should be noted that an NHS England Commissioning through Evaluation process is currently examining selective dorsal rhizotomy, which has affected availability of NHS-funding for the procedure. A decision is unlikely until 2017/2018.

New evidence is unlikely to change guideline recommendations.

Selective dorsal rhizotomy

145 – 10 What is the clinical effectiveness of selective dorsal rhizotomy in children and young people with spasticity caused by a non-progressive brain disorder?

Recommendations derived from this question

1.8.1 Consider selective dorsal rhizotomy to improve walking ability in children and young people with spasticity at GMFCS level II or III:

- Patient selection and treatment should be carried out by a multidisciplinary team with specialist training and expertise in the care of spasticity, and with access to the full range of treatment options.
- Discuss the irreversibility of the treatment, the known complications and the uncertainties over long-term outcomes with children and young people, and their parents and/or carers (see also Selective dorsal rhizotomy for spasticity in cerebral palsy, NICE interventional procedure guidance 373).
- Teams offering selective dorsal rhizotomy should participate in a coordinated national agreed programme to collect information on short- and long-term outcomes on all patients assessed for selective dorsal rhizotomy, whether or not selective dorsal rhizotomy is performed. These recorded outcomes should include measures of muscle tone, gross motor function, neurological impairment, spinal deformity, quality of life and need for additional operations, with nationally agreed consistent definitions.

Surveillance decision

This review question should not be updated.

Predictors for the benefit of selective dorsal rhizotomy

2-year Evidence Update

No relevant evidence was identified.

4-year surveillance summary

A prospective cohort study[40] (n=54) examined predictors for the benefit of selective dorsal rhizotomy in ambulatory children (mean age 6.9 years) with spastic cerebral palsy. Spasticity on the Modified Ashworth Scale of hip adductors and hamstrings decreased significantly and stayed reduced after two years, while GMFM improved significantly 12 months after selective dorsal rhizotomy and further significantly improved between 12 and 24 months. Muscle strength improved significantly concerning knee extension and ankle dorsiflexion. The improvement of function correlated moderately with age at surgery (most benefit in children aged 4–7 years) and preoperative GMFM (most benefit between 65% and 85%) and weakly with the standard deviation score of the BMI, the dorsiflexor and plantarflexor strength preoperatively as well as with the reduction of spasticity of the hamstrings and the preoperative spasticity of the adductors and hamstrings.

Topic expert feedback

The topic experts stated that being able to predict which children would benefit from an irreversible procedure would be helpful. Some limitations of the study were noted, such as the lack of a control group, the relatively short follow up, and the population of GMFCS I and II (which does not align with the anticipated population of GMFCS II and III in the recommendations and research recommendation in CG145).

The topic experts also drew attention to the NHS England project of Commissioning through Evaluation of selective dorsal rhizotomy, which has affected availability of NHS funding for the procedure. They stated that there was unlikely to be a decision until 2017/2018.

Impact statement

The new evidence suggests that selective dorsal rhizotomy appears to reduce spasticity and increase motor skills for at least up to 2 years in children with spastic cerebral palsy corresponding to changes in GMFM that the authors stated were clinically relevant, without compromising muscular strength. The data further suggest that children who benefit the most from selective dorsal rhizotomy are aged 4–7 years and have a preoperative GMFM between 65% and 85%.

NICE CG145 recommends considering selective dorsal rhizotomy to improve walking ability in children and young people with spasticity at GMFCS level II or III. It also adopts the recommendation from IPG373 'Selective dorsal rhizotomy for spasticity in cerebral palsy' that patient selection and treatment should be carried out by a multidisciplinary team with specialist training and expertise in the care of spasticity, though CG145 does not currently make any recommendations specifically related to suitability of patients based on age or motor function.

The new evidence is from a small study with several limitations, and further studies are needed to confirm the results, therefore this evidence is currently unlikely to impact the guideline.

It should also be noted that an NHS England Commissioning through Evaluation process is currently examining selective dorsal rhizotomy, which has affected availability of NHS-funding for the procedure. Any changes to the recommendations in CG145 on selective dorsal rhizotomy would ideally be informed by the outcome of this process, which is unlikely to be published until 2017/2018.

New evidence is unlikely to change guideline recommendations.

Long-term outcome after selective dorsal rhizotomy

2-year surveillance summary

No relevant evidence was identified.

4-year surveillance summary

A retrospective review of a prospective database[41] (n=44) examined long-term outcomes after selective dorsal rhizotomy in children (mean age 4.5 years at surgery) with spastic cerebral palsy. Patients were stratified by GMFCS level into group 1 (GMFCS II and III) and group 2 (GMFCS IV and V). Assessments were performed pre-operatively, at 6 months to 5 years, and more than 10 years postoperatively. Patients were followed for a mean of 14.4 years. Spasticity on the Modified Ashworth Scale significantly decreased by early postoperative evaluation with further decrease at late evaluation. Early significant improvement in hip range of motion was not sustained at late assessment. Motor function improved in both groups at early assessment but was only sustained in group 1. Group 1 significantly increased by 10 points at early evaluation but subsequently decreased by 3.5, resulting in an overall significant increase of 6.6 from baseline. Group 2 patients had an initial significant increase of 8.3 but then declined to 4.9 below baseline.

A prospective cohort study[42] (n=18) investigated long-term effects 15–20 years after selective dorsal rhizotomy in children (mean age at surgery 4.6 years) with bilateral spastic cerebral palsy. The effect of normalised muscle tone in lower extremities after selective dorsal rhizotomy was sustained after a median of 17 years. The best gross motor function capacity, according to the GMFM score, was seen at the 3-year follow-up, thereafter a gradual decline followed. Half of the individuals reported low intensity pain and interference. Compared to a norm sample the physical health component of the Short Form (36) Health Survey v2 was slightly lower and the mental health component slightly higher.

Topic expert feedback

The topic experts noted that these studies help answer the question about long term effect of selective dorsal rhizotomy on mobility highlighted in the research recommendation. Some limitations of the studies were noted. The retrospective review had a large loss to follow up and those missing may have had poorer outcomes, potentially biasing results. The prospective cohort was very small, however it evaluated pain and quality of life which was noted to be of particular importance.

The topic experts also drew attention to the NHS England project of Commissioning

through Evaluation of selective dorsal rhizotomy, which has affected availability of NHS funding for the procedure. They stated that there was unlikely to be a decision until 2017/2018.

Impact statement

New evidence from 2 studies with several limitations suggests that selective dorsal rhizotomy appears to have long-term effects on reducing spasticity that persist for at least 17 years. However early improvements in motor function do not appear to be sustained, particularly among those with a higher GMFCS of IV or V. The authors of the second study stated that the intervention can possibly reduce the pain often experienced by individuals with cerebral palsy. This evidence appears to be consistent with the recommendation in CG145 to consider selective dorsal rhizotomy to improve walking ability in children and young people with spasticity at GMFCS level II or III. It also goes some way towards answering the priority research recommendation 'Does selective dorsal rhizotomy followed by intensive rehabilitation performed between the ages of 3 and 9 years in children who are at GMFCS level II or III result in good community mobility as a young adult?'

It should be noted, however, that an NHS England Commissioning through Evaluation process is currently examining selective dorsal rhizotomy, which has affected availability of NHS-funding for the procedure. A decision is unlikely until 2017/2018.

New evidence is unlikely to change guideline recommendations.

Single event multilevel muscle tendon surgery, osteotomies, and dorsal rhizotomy

2-year Evidence Update

No relevant evidence was identified.

4-year surveillance summary

A retrospective cohort study[39] (n=94) compared effects of single-event multilevel muscle tendon surgery, osteotomies, and dorsal rhizotomy for children aged 4–18 years with cerebral palsy (GMFCS classification I–III).

Topic expert feedback

Expert feedback is discussed in the entry for this study in the previous review question (145–09).

Impact statement

Details of the study and its impact on CG145 are discussed in the entry for this study in the previous review question (145–09).

New evidence is unlikely to change guideline recommendations

NQ – 01 **What is the effectiveness of magnetic stimulation, electrical stimulation, vibration training, and shock wave therapy as compared to other interventions at reducing spasticity, maintaining motor function and preventing secondary complications in children with spasticity and with or without other motor disorders (dystonia, muscle weakness and choreoathetosis) caused by a non-progressive brain disorder?**

This question was not addressed by the guideline.

Surveillance decision

This question should not be added.

Repetitive transcranial magnetic stimulation (rTMS)

2-year Evidence Update

No relevant evidence was identified.

4-year surveillance summary

Two reports[43,44] from a double-blinded RCT (n=19) examined efficacy and safety of primed low-frequency rTMS in the contralesional hemisphere plus constraint-induced movement therapy (CIMT) to promote recovery of the paretic hand in children aged 8–17 years with congenital paediatric hemiparesis (Manual Ability Classification Scale levels I-III). Children underwent 5 sessions of either real 6 Hz primed, low-frequency rTMS or sham, and each group alternated daily with CIMT. CIMT consisted of 13 days of continuous long-arm casting with 5 skin-check sessions. Each child received a total of 10 hours of one-to-one therapy.

In the first report[43], improvements were seen in the primary outcome of Assisting Hand Assessment that differed significantly between groups. No significant differences in the secondary outcome measures (Canadian Occupational Performance Measure, and stereognosis) were found. Significantly more participants in the rTMS group showed improvement greater than the smallest detectable difference of 4 points than in the sham group. No serious adverse events occurred.

In the second report[44], no major adverse events were observed. Minor adverse events were found in both groups. The most common events were headaches and cast irritation, which did not differ significantly between groups. No differences between groups in secondary cognitive and unaffected hand motor measures were found.

An assessor-blinded RCT[45] (n=45) examined whether the addition of rTMS and/or CIMT to intensive therapy increased motor function in children aged 6–19 years with perinatal stroke and hemiparesis. All children completed a 2-week, goal-directed, peer-supported motor learning camp and were randomised to daily rTMS, CIMT, both, or neither. Intention-to-treat analysis examined treatment effects over time (linear mixed effects model). Addition of rTMS, CIMT, or both doubled the chances of clinically significant improvement. Gains in the primary outcome of Assisting Hand Assessment at 6 months were additive, and the largest significant gain was with rTMS + CIMT. The camp alone produced large significant improvements in the other primary outcome of Canadian Occupational Performance Measure scores, maximal at 6 months. Quality-of-life scores improved (significance not stated in the abstract). Interventions were well tolerated and safe with no decrease in function of either hand.

Topic expert feedback

No topic expert feedback was relevant to this evidence.

Impact statement

New evidence from 2 studies suggests that primed, low-frequency rTMS combined with CIMT appears to be a potentially safe and effective intervention that can achieve sustained improvement in hand function in congenital pediatric hemiparesis. CG145 does not make any recommendations on rTMS. However, the new evidence is from small RCTs that did not examine the long-term effects of the intervention. This evidence is therefore unlikely to affect the guideline.

New evidence is unlikely to impact on the guideline.

Transcranial electrical stimulation

2-year Evidence Update

No relevant evidence was identified.

4-year surveillance summary

A pilot double-blind RCT[46] (n=20) examined effects of anodal transcranial direct current stimulation combined with virtual reality training for improving gait in children with spastic diparetic cerebral palsy. The experimental group received anodal stimulation and the control group received sham stimulation over the primary motor cortex during virtual reality training. All patients underwent the same training programme involving virtual reality (10 sessions). Evaluations were performed before and after the intervention and at 1-month follow-up. The experimental group had a better performance regarding gait velocity, cadence, gross motor function, and

independent mobility (significance not stated in the abstract). Moreover, transcranial direct current stimulation led to a significant increase in motor evoked potential.

Topic expert feedback

No topic expert feedback was relevant to this evidence.

Impact statement

The new evidence suggests that anodal transcranial direct current stimulation combined with virtual reality training could provide functional benefit in children with spastic cerebral palsy. CG145 does not make any recommendations on this intervention, however the authors noted that these were preliminary findings and are therefore unlikely to impact the guideline. Further research is needed to confirm the results.

New evidence is unlikely to impact on the guideline.

Functional electrical stimulation (FES) of ankle dorsiflexors

2-year Evidence Update

No relevant evidence was identified.

4-year surveillance summary

An RCT[47] (n=32) examined orthotic and therapeutic effects following daily community-applied FES to the ankle dorsiflexors in children (mean age 10.3 years) with unilateral spastic cerebral palsy (GMFCS I–II). Treatment group: 8 weeks of daily FES (4 hours per day, 6 days per week) via a device attached to the leg. Control group: usual orthotic and therapy treatment. Children were assessed at baseline, post FES treatment (8 weeks) and follow-up (6 weeks after post FES treatment). FES led to a significant increase in initial contact ankle angle, maximum dorsiflexion ankle angle in swing, normalised time in stance, and normalised step length compared to controls. Once FES was removed, the treatment group significantly increased community mobility balance scores at post treatment and at follow-up compared to controls. The treatment group also had significantly reduced gastrocnemius spasticity at post treatment and at follow-up compared to the control group.

Topic expert feedback

No topic expert feedback was relevant to this evidence.

Impact statement

The new evidence suggests that FES seems to have an orthotic effect with improvement in lower limb mechanics during gait. Therapeutic effects, that is, without the FES device, were observed in gastrocnemius spasticity, community mobility and balance skills in the treatment group at post treatment and follow-up. CG145 does not make recommendations on FES of ankle dorsiflexors, however this evidence is from 1 small trial and is therefore currently unlikely to affect the guideline. Further research is needed to confirm the results.

New evidence is unlikely to impact on the guideline.

Whole-body vibration training

2-year Evidence Update

No relevant evidence was identified.

4-year surveillance summary

An RCT[48] (n=30) investigated the effects of whole-body vibration training on muscle strength and balance in children with diplegic cerebral palsy. The experimental group received whole-body vibration training (9 mins per day, 5 days per week) and the control group had a traditional physical therapy exercise programme for 3 successive months. The experimental group showed a significantly higher peak torque on the Biodex isokinetic dynamometer at 60 degrees per second and 90 degrees per second after treatment. Outcomes with the overall stability index in the experimental group were numerically superior (significance not stated in the abstract).

A systematic review and meta-analysis[49] of 6 RCTs (n=176) evaluated the effects of whole body vibration versus exercise and/or control on mobility and balance in children with cerebral palsy. Whole-body vibration resulted in significant improvements in gait speed, gross motor function dimension E, and femur bone density. There was a non-significant difference

in muscle strength and gross motor function dimension D for participants in the whole-body vibration compared with control group. No serious adverse events were reported.

Topic expert feedback

No topic expert feedback was relevant to this evidence.

Impact statement

New evidence from 2 studies suggests that whole-body vibration training may improve muscle strength, balance, gait speed and standing function in children with cerebral palsy. Although CG145 does not make any recommendations on whole-body vibration training, more evidence on the long-term effects of the intervention, and more functional outcome data, would be useful. This evidence is therefore currently unlikely to affect the guideline.

New evidence is unlikely to impact on the guideline.

Extracorporeal shock wave therapy

2-year Evidence Update

No relevant evidence was identified.

4-year surveillance summary

An RCT[50] (n=30) investigated the effects of extracorporeal shock wave therapy on gait pattern in children with hemiplegic cerebral palsy. The study group received shock wave therapy (1500 shots/muscle, frequency of 5Hz, energy of 0.030 mJ/mm, 1 session per week). The control group participated in a conventional physical therapy exercise programme for 3 successive months. The study group showed a significantly greater improvement in spasticity on the Modified Ashworth Scale after treatment than the control group. The significance of differences between groups for the gait parameters of stride length, cadence, speed, cycle time, and stance phase percentage were not reported in the abstract.

Topic expert feedback

No topic expert feedback was relevant to this evidence.

Impact statement

The new evidence suggests that shock wave therapy may improve spasticity in children with hemiplegic cerebral palsy. CG145 does not make recommendations on shock wave therapy, however the evidence is from a single small trial and therefore unlikely to currently affect the guideline. Further research is needed to confirm the results.

New evidence is unlikely to impact on the guideline.

NQ – 02 What is the effectiveness of umbilical cord blood cell therapy in the treatment of spasticity and other motor disorders (dystonia, muscle weakness and choreoathetosis) caused by a non-progressive brain disorder in children and young people?

This question was not addressed by the guideline.

Surveillance decision

This question should not be added.

Umbilical cord blood cell therapy

2-year Evidence Update

No relevant evidence was identified.

4-year surveillance summary

A double-blind RCT[51] (n=36) evaluated the efficacy of umbilical cord blood versus placebo for people aged 6 months–20 years with

cerebral palsy. The umbilical cord blood group showed significantly greater improvements in muscle strength than controls at 1 and 3 months after treatment. The umbilical cord blood group also showed significantly greater improvements in gross motor performance than the control group at 6 months after treatment. Generally, motor outcomes were positively correlated with the number of umbilical cord blood cells administered (significance not reported in abstract). Additionally, positron emission tomography scans revealed decreased periventricular inflammation in patients administered umbilical cord blood, compared with those treated with a placebo. Correlating with enhanced gross motor function, elevations in plasma pentraxin 3 and interleukin-8 levels were observed for up to 12 days after treatment in the umbilical cord blood group. Meanwhile, increases in blood cells expressing Toll-like receptor 4 were noted at 1 day after treatment in the umbilical cord blood group, and they were correlated with increased muscle strength at 3 months post-treatment.

Topic expert feedback

No topic expert feedback was relevant to this evidence.

Impact statement

The new evidence suggests that treatment with umbilical cord blood could improve motor outcomes in cerebral palsy. CG145 does not make any recommendations on the use of umbilical cord blood. However, the authors stated that future trials are needed to confirm the long-term efficacy of umbilical cord blood therapy, as the follow-up duration of the trial was short. Therefore, this evidence is currently unlikely to affect the guideline.

New evidence is unlikely to impact on the guideline.

NQ – 03 What is the most effective management strategy for scoliosis and kyphosis in children and young people with spasticity caused by a non-progressive brain disorder?

This question was not addressed by the guideline.

Surveillance decision

This question should not be added.

Surgical correction of scoliosis

2-year Evidence Update

No relevant evidence was identified.

4-year surveillance summary

A systematic review[52] of 14 studies (10 case series, 1 prospective and 3 retrospective cohort studies) examined the benefits, adverse effects, and preoperative factors affecting patient outcome after surgical correction of scoliosis in children with spastic quadriplegia. No data on benefits of surgery were reported in the abstract. There was significant variation in the overall risk of complications (range, 11–71%), mortality (range, 3–19%), respiratory/pulmonary complications (range, 27–57%), and infection (range, 2.5–56.8%). Caregivers report a high degree of satisfaction with scoliosis surgery for children with spastic quadriplegia. There is limited evidence of preoperative factors that can predict patient outcome after scoliosis, but factors associated with a worse outcome were a significant degree of thoracic kyphosis, days in the intensive care unit, and poor nutritional status.

Topic expert feedback

During a quarterly review meeting of the National Collaborating Centre for Women's and Children's Health, and subsequently at a committee meeting for the forthcoming cerebral palsy in children and young people guideline, topic experts noted that scoliosis – prevention and management in children and young people with spasticity – was not covered in CG145, nor

will it be covered in the in-development NICE guideline on cerebral palsy in children and young people. At these meetings it was suggested that scoliosis could potentially be added to CG145 at its next surveillance review. Among the reasons stated for adding this to CG145 were that scoliosis is more closely related to spasticity, and more people have scoliosis without cerebral palsy than with.

Some experts felt it was a serious omission given that it results from the motor impairment in the same way that hip displacement (which was included) does. It has a major impact on the health and well-being of young people with spasticity. The cerebral palsy guideline is focusing on the co-morbidities so it was not appropriate to bring scoliosis into this guideline either but the view was that it might be included in a review of spasticity.

Impact statement

Topic experts felt that scoliosis should be considered in CG145, particularly given that the in-development NICE guideline on cerebral palsy in children and young people is not expected to make recommendations on this condition.

However, the new evidence identified was not sufficient to suggest the new question should be added to CG145. The evidence showed wide variation in the overall risk of complications of scoliosis surgery in spastic quadriplegia, but did not report efficacy data which prevents any firm conclusions and therefore no impact of this evidence on CG145 (in which management of scoliosis is out of scope) is expected. The authors noted that there is a need for well-designed prospective studies of scoliosis surgery in this population.

Additionally, it should be noted that scoliosis can be caused by conditions other than spasticity, and most cases are idiopathic. CG145 may not therefore be the most appropriate place for guidance on scoliosis.

This area will be monitored by future surveillance.

Current NICE guidance in this area includes MTG18 'The MAGEC system for spinal lengthening in children with scoliosis'.

New evidence is unlikely to impact on the guideline.

NQ – 04 What is the most effective management strategy for children and young people with a pure dystonic tone abnormality caused by a non-progressive brain disorder?

This question was not addressed by the guideline.

Surveillance decision

This question should not be added.

Pure dystonic tone abnormality

2-year Evidence Update

No relevant evidence was identified.

4-year surveillance summary

No relevant evidence was identified.

Topic expert feedback

It was noted in a scoping meeting for the forthcoming cerebral palsy in children and young people guideline, that dystonia in the absence of spasticity was not a priority in a very full scope for cerebral palsy. However it was suggested that dystonia could potentially be added to CG145 at its next surveillance review.

Topic experts noted that children with a pure dystonic tone abnormality are excluded from CG145 and their tone management is not covered in the in-development NICE guideline on cerebral palsy in children and young people. Therefore no existing or planned guideline covers dystonia in children.

Impact statement

Topic experts felt that pure dystonic tone abnormality should be considered in CG145, particularly given that the in-development guideline on cerebral palsy in children and young people is not expected to make recommendations on this condition.

However, no evidence was identified therefore no impact on CG145 (in which pure dystonic tone is out of scope) is expected. Additionally dystonias are not limited to people with spasticity. CG145 may not therefore be the most appropriate place for guidance on dystonia, as this could only cover dystonia in patients with spasticity.

This area will be monitored by future surveillance.

Current NICE guidance in this area includes IPG188 'Deep brain stimulation for tremor and dystonia (excluding Parkinson's disease)'.

New evidence is unlikely to impact on the guideline.

NQ – 05 What is the most effective measurement of spasticity and function in children and young people with spasticity caused by a non-progressive brain disorder?

This question was not addressed by the guideline.

Surveillance decision

This question should not be added.

Measurement of spasticity and function

2-year Evidence Update

No relevant evidence was identified.

4-year surveillance summary

No relevant evidence was identified.

Topic expert feedback

Topic experts noted that measurement of spasticity was not covered in the guideline. The Ashworth score is probably the commonest method. The Tardieu scale is more difficult to do but probably is more objective and reliable.

They further noted that objective clinical assessment tools had been enhanced by the introduction of the Quality FM (Quality Function Measure) which supplements GMFM.

Impact statement

Topic experts felt that measurement of spasticity and function should be considered in CG145.

However, no evidence was identified to support the addition of the new question to the guideline, therefore no impact is anticipated. Additionally, measurement of spasticity is currently outside the remit of the guideline.

New evidence is unlikely to impact on the guideline.

NQ – 06 Age up to 25 years

Management of spasticity in people aged 19–25 years was not addressed by the guideline.

Surveillance decision

The guideline scope should not be extended to include age up to 25 years.

Age up to 25 years

2-year Evidence Update

No relevant evidence was identified.

4-year surveillance summary

No relevant evidence was identified.

Topic expert feedback

Topic experts noted that the scope of the in-development NICE guideline on cerebral palsy in children and young people goes up to age 25, in line with the Children and Families Act 2014 (in which the section on children and young people in England with special educational needs or disabilities notes that 'young person' means a person over compulsory school age but under 25). The experts felt it would therefore make sense to do the same with CG145, but suspected it might be challenging, given how paediatric services are configured in the UK.

It was noted that in the population covered by CG145, the original neurological lesion does not change but its impact changes over time. There are 2 groups in particular whose physical presentation continues to change between 18 and 25 years:

1. Those with some ability to walk but who lose this ability in adolescence and early adulthood. There are questions about whether this is inevitable, or if mobility could be maintained with appropriate therapy. Motor ability often deteriorates after transition to adult services but it is not clear if this could be due to reduced resources compared to children's services, or whether it is an inevitable part of the 'natural history'.

2. Those with severe spasticity who are now living longer. This leads to physiological changes not previously seen (such as respiratory and circulatory problems, deterioration in swallowing ability, increased reflux, and emerging autonomic dysfunctions) which may arise from severe postural distortions resulting from spasticity. Following transfer of care from paediatricians to GPs, symptoms might be misinterpreted and inappropriately acted on. For example, a cough may not be a chest infection but a change in reflux or swallowing. Vomiting may not be gastroenteritis but reflux, severe constipation or reduced space for abdominal contents due to posture changes. Raised temperature and pulse may not be an infection but an autonomic dysfunction.

Impact statement

One topic expert felt that the scope of CG145 should be extended to people aged up to 25 years. Age up to 25 years is currently outside the remit of the guideline.

However, no evidence was identified to support the extension of the scope. Increasing the age limit of the guideline introduces some questions about managing long-term aspects of spasticity. Currently it is not clear how much evidence is available on this to inform recommendations. As a result, no impact is anticipated at the moment. NICE is currently developing a guideline for cerebral palsy in adults. Although this will cover ages 25 and over, the management of spasticity in people aged 19 and over with cerebral palsy has been proposed in the first draft of the scope of the cerebral palsy in adults guideline.

This area will be monitored by future surveillance, and will be considered when an update to the guideline is needed.

New evidence is unlikely to impact on the guideline.

Research recommendations

Prioritised research recommendations

At 4-year and 8-year surveillance reviews of guidelines published after 2011, we assess progress made against prioritised research recommendations. We may then propose to remove research

recommendations from the NICE version of the guideline and the NICE database for research recommendations. The research recommendations will remain in the full version of the guideline. See NICE's research recommendations process and methods guide 2015 for more information.

These research recommendations were deemed priority areas for research by the Guideline Committee; therefore, at this 4-year surveillance review time point a decision **will** be taken on whether to retain the research recommendations or stand them down.

We applied the following approach:

- New evidence relevant to the research recommendation was found and an update of the related review question is planned.
  - The research recommendation will be removed from the NICE version of the guideline and the NICE research recommendations database. If needed, a new research recommendation may be made as part of the update process.
- New evidence relevant to the research recommendation was found but an update of the related review question is not planned because the new evidence is insufficient to trigger an update.
  - The research recommendation will be retained because there is evidence of research activity in this area.
- New evidence relevant to the research recommendation was found but an update of the related review question is not planned because evidence supports current recommendations.
  - The research recommendation will be removed from the NICE version of the guideline and the NICE research recommendations database because further research is unlikely to impact on the guideline.
- Ongoing research relevant to the research recommendation was found.
  - The research recommendation will be retained and evidence from the ongoing research will be considered when results are published.
- No new evidence relevant to the research recommendation was found and no ongoing studies were identified.
  - The research recommendation will be removed from the NICE version of guideline and the NICE research recommendations database because there is no evidence of research activity in this area.
- The research recommendation would be answered by a study design that was not included in the search (usually systematic reviews or randomised controlled trials).
  - The research recommendation will be retained in the NICE version of the guideline and the NICE research recommendations database.
- The new research recommendation was made during a recent update of the guideline.
  - The research recommendation will be retained in the NICE version of the guideline and the NICE research recommendations database.

RR – 01 What are the greatest inhibitors of functional ability in children and young people with upper motor neurone lesions?

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

Surveillance decision

It was proposed to remove the research recommendation from the NICE version of guideline and the NICE research recommendations database because there is no evidence of research activity in this area. We considered the views of stakeholders after consultation. Therefore it was decided to retain this research recommendation based on the feedback on its importance.

RR – 02 **What is the optimal postural management programme using a standing frame in children aged 1–3 years?**

New evidence relevant to the research recommendation was found but an update of the related review question is not planned because evidence supports current recommendations.

Surveillance decision

The research recommendation will be removed from the NICE version of the guideline and the NICE research recommendations database because further research is unlikely to impact on the guideline.

RR – 03 **What is the clinical and cost effectiveness of botulinum toxin type A when used routinely or according to clinical need in children and young people who are at GMFCS level I, II or III?**

New evidence relevant to the research recommendation was found but an update of the related review question is not planned because the new evidence is insufficient to trigger an update.

Surveillance decision

The research recommendation will be retained because there is evidence of research activity in this area.

RR – 04 **What is the clinical and cost effectiveness of continuous pump-administered intrathecal baclofen compared with usual care in children and young people who are at GMFCS level IV or V?**

New evidence relevant to the research recommendation was found but an update of the related review question is not planned because the new evidence is insufficient to trigger an update.

Surveillance decision

The research recommendation will be retained because there is evidence of research activity in this area.

RR – 05 **Does selective dorsal rhizotomy followed by intensive rehabilitation performed between the ages of 3 and 9 years in children who are at GMFCS level II or III result in good community mobility as a young adult?**

Ongoing research relevant to the research recommendation was found (although the Commissioning through Evaluation process will not answer the question of long term outcomes, the participating centres will have a cohort that could be followed up).

Surveillance decision

The research recommendation will be retained and evidence from the ongoing research will be considered when results are published.

Other research recommendations

The following research recommendations were not deemed as priority areas for research by the guideline committee. No decisions will be taken the status of these research recommendations.

RR – 06 **What is the clinical and cost effectiveness of 24-hour postural management programmes in non-ambulatory children and young people with bilateral spasticity affecting all four limbs?**

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

RR – 07 **What is the optimal duration for the passive stretch component of physical therapy?**

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

RR – 08 **What is the clinical and cost effectiveness of activity-based context-focused physical therapy compared with child-focused physical therapy in children and young people who are at GMFCS level I, II or III?**

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

RR – 09 **What is the clinical and cost effectiveness and optimal age for modified constraint-induced movement therapy?**

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

RR – 10 **What is the clinical and cost effectiveness of a prolonged stretch of the calf muscles with a hinged ankle-foot orthosis compared to an ankle-foot orthosis worn for a shorter time in children and young people with unilateral spasticity affecting the leg?**

New evidence relevant to the research recommendation was found but an update of the related review question is not planned because the new evidence is insufficient to trigger an update.

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

RR – 11 **What is the clinical and cost effectiveness of wearing a hinged ankle-foot orthosis to prevent an equinus foot posture compared to an ankle-foot orthosis or solid ankle-foot orthosis?**

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

RR – 12 **What is the clinical and cost effectiveness of wearing an ankle-foot orthosis after surgery compared to not wearing an ankle-foot orthosis in children and young people with lower limb spasticity?**

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

RR – 13 **What is the clinical and cost effectiveness of dynamic thermoplastic orthoses compared to static orthoses in children and young people with unilateral spasticity affecting the arm who have abnormal posturing?**

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

RR – 14 **What is the clinical and cost effectiveness of a spinal orthosis compared to no orthosis when not in a supportive chair in children and young people with low tone and peripheral spasticity?**

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

RR – 15 **What is the clinical and cost effectiveness of night-time oral baclofen or oral diazepam combined with physical therapy compared to physical**

therapy only in children and young people who are at GMFCS level I, II, III, IV or V?

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

RR – 16 **What is the clinical and cost effectiveness of night-time oral baclofen or oral diazepam combined with physical therapy and a night-time postural control system compared to physical therapy and a night-time postural control system only in children and young people who are at GMFCS level I, II, III, IV or V?**

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

RR – 17 **What is the comparative clinical and cost effectiveness of oral trihexyphenidyl, levodopa and baclofen in improving pain, positioning, and motor skills in children and young people with significant dystonia as a symptom of their non-progressive brain disorder?**

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

RR – 18 **What is the clinical and cost effectiveness of treatment with botulinum toxin type A combined with a 6-week targeted strengthening programme compared to a 6-week targeted strength training programme only in school-aged children and young people with lower limb spasticity who are at GMFCS level I, II or III?**

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

RR – 19 **What is the clinical and cost effectiveness of botulinum toxin type A for reducing muscle pain?**

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

RR – 20 **What is the clinical and cost effectiveness of botulinum toxin type A compared to botulinum toxin type B for reducing spasticity while minimising side effects?**

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

RR – 21 **What is the predictive accuracy of intrathecal baclofen testing for identifying those children and young people who respond well to continuous pump-administered intrathecal baclofen treatment?**

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

RR – 22 **What is the clinical and cost effectiveness of continuous pump-administered intrathecal baclofen in terms of improving functional outcomes in children and young people who are at GMFCS level II?**

New evidence relevant to the research recommendation was found but an update of the related review question is not planned because the new evidence is insufficient to trigger an update.

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

RR – 23 **What is the clinical and cost effectiveness of gait analysis as an assessment tool in studies to evaluate interventions such as continuous pump-administered intrathecal baclofen?**

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

RR – 24 **What is the clinical and cost effectiveness of soft tissue surgery in terms of preventing hip dislocation?**

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

RR – 25 **What is the clinical and cost effectiveness of single-event multilevel surgery in terms of producing benefits that continue after skeletal maturity has been achieved?**

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

RR – 26 **What is the clinical and cost effectiveness of selective dorsal rhizotomy compared to continuous pump-administered intrathecal baclofen in children and young people who are at GMFCS level IV or V?**

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

References

1. Hagglund G, Alriksson-Schmidt A, Lauge-Pedersen H et al. (2014) Prevention of dislocation of the hip in children with cerebral palsy: 20-year results of a population-based prevention programme. Bone Joint J 96-B:1546-1552.

2. Paleg GS, Smith BA, and Glickman LB. (2013) Systematic review and evidence-based clinical recommendations for dosing of pediatric supported standing programs. Pediatr Phys Ther 25:232-247.

3. El-Basatiny HM and Abdel-Aziem AA. (2015) Effect of backward walking training on postural balance in children with hemiparetic cerebral palsy: a randomized controlled study. Clinical Rehabilitation 29:457-467.

4. 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. J Child Neurol 27:992-999.

5. 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. Neurorehabil.Neural Repair 25:692-702.

6. Chen YP, Pope S, Tyler D et al. (2014) Effectiveness of constraint-induced movement therapy on upper-extremity function in children with cerebral palsy: a systematic review and meta-analysis of randomized controlled trials. [Review]. Clinical Rehabilitation 28:939-953.

7. Sakzewski L, Miller L, Ziviani J et al. (2015) Randomized comparison trial of density and context of upper limb intensive group versus individualized occupational therapy for children with unilateral cerebral palsy. Developmental Medicine & Child Neurology 57:539-547.

8. 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. Am J Phys Med Rehabil 91:747-760.

9. Bania TA, Dodd KJ, Baker RJ et al. (2016) The effects of progressive resistance training on daily physical activity in young people with cerebral palsy: a randomised controlled trial. Disability & Rehabilitation 38:620-626.

10. Van Wely L., Balemans AC, Becher JG et al. (2014) Physical activity stimulation program for children with cerebral palsy did not improve physical activity: a randomised trial. Journal of Physiotherapy 60:40-49.

11. Van Wely L., Balemans AC, Becher JG et al. (2014) The effectiveness of a physical activity stimulation programme for children with cerebral palsy on social participation, self-perception and quality of life: a randomized controlled trial. Clinical Rehabilitation 28:972-982.

12. Slaman J, Roebroeck M, Dallmijer A et al. (2015) Can a lifestyle intervention programme improve physical behaviour among adolescents and young adults with spastic cerebral palsy? A randomized controlled trial. Developmental Medicine & Child Neurology 57:159-166.

13. Slaman J, van den Berg-Emons HJ, van MJ et al. (2015) A lifestyle intervention improves fatigue, mental health and social support among adolescents and young adults with cerebral palsy: focus on mediating effects. Clinical Rehabilitation 29:717-727.

14. Slaman J, Berg-Emons R, Tan SS et al. (2015) Cost-utility of a lifestyle intervention in adolescents and young adults with spastic cerebral palsy. Journal of Rehabilitation Medicine 47:338-345.

15. Franki I, Van den Broeck C, De CJ et al. (2014) A randomized, single-blind cross-over design evaluating the effectiveness of an individually defined, targeted physical therapy approach in treatment of children with cerebral palsy. Clinical Rehabilitation 28:1039-1052.

16. Franki I, Desloovere K, De CJ et al. (2015) An evaluator-blinded randomized controlled trial evaluating therapy effects and prognostic factors for a general and an individually defined physical therapy program in ambulant children with bilateral spastic cerebral palsy. European journal of physical & rehabilitation medicine 51:677-691.

17. Chiu HC, Ada L, and Lee HM. (2014) Upper limb training using Wii Sports Resort for children with hemiplegic cerebral palsy: a randomized, single-blind trial. Clinical Rehabilitation 28:1015-1024.

18. 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. Am J Phys Med Rehabil 92:905-911.

19. Bjornson K, Zhou C, Fatone S et al. (2016) The Effect of Ankle-Foot Orthoses on Community-Based Walking in Cerebral Palsy: A Clinical Pilot Study. Pediatric Physical Therapy 28:179-186.

20. Maas JC, Huijing PA, Dallmeijer AJ et al. (2015) Decrease in ankle-foot dorsiflexion range of motion is related to increased knee flexion during gait in children with spastic cerebral palsy. Journal of Electromyography & Kinesiology 25:339-346.

21. Roberts A, Wales J, Smith H et al. (2016) A randomised controlled trial of laser scanning and casting for the construction of ankle-foot orthoses. Prosthetics and Orthotics International.40 (2) (pp 253-261), 2016.Date of Publication: April 2016. 253-261.

22. Martins E, Cordovil R, Oliveira R et al. (2016) Efficacy of suit therapy on functioning in children and adolescents with cerebral palsy: A systematic review and meta-analysis. Developmental Medicine and Child Neurology.58 (4) (pp 348-360), 2016.Date of Publication: 01 Apr 2016. 348-360.

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

24. Pozin I, Bdolah-Abram T, and Ben-Pazi H. (2014) Levodopa does not improve function in individuals with dystonic cerebral palsy. Journal of Child Neurology 29:534-537.

25. Baker JA and Pereira G. (2015) The efficacy of Botulinum Toxin A on improving ease of care in the upper and lower limbs: a systematic review and meta-analysis using the Grades of Recommendation, Assessment, Development and Evaluation approach. Clin Rehabil 29:731-740.

26. Delgado MR, Tilton A, Russman B et al. (2016) AbobotulinumtoxinA for Equinus Foot Deformity in Cerebral Palsy: A Randomized Controlled Trial. Pediatrics 137:1-9.

27. Kahraman A, Seyhan K, Deger U et al. (22-4-2016) Should botulinum toxin A injections be repeated in children with cerebral palsy? A systematic review. Dev Med Child Neurol .

28. Van Campenhout A., Bar-On L, Desloovere K et al. (2015) Motor endplate-targeted botulinum toxin injections of the gracilis muscle in children with cerebral palsy. Developmental Medicine & Child Neurology 57:476-483.

29. Copeland L, Edwards P, Thorley M et al. (2014) Botulinum toxin A for nonambulatory children with cerebral palsy: a double blind randomized controlled trial. Journal of Pediatrics 165:140-146.

30. Ferrari A, Maoret AR, Muzzini S et al. (2014) A randomized trial of upper limb botulimun toxin versus placebo injection, combined with physiotherapy, in children with hemiplegia. Research in Developmental Disabilities 35:2505-2513.

31. Lidman G, Nachemson A, Peny-Dahlstrand M et al. (2015) Botulinum toxin A injections and occupational therapy in children with unilateral spastic cerebral palsy: a randomized controlled trial. Developmental Medicine & Child Neurology 57:754-761.

32. 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. Dev Med Child Neurol 54:743-747.

33. Edwards P, Sakzewski L, Copeland L et al. (2015) Safety of Botulinum Toxin Type A for Children With Nonambulatory Cerebral Palsy. Pediatrics 136:895-904.

34. Carraro E, Trevisi E, and Martinuzzi A. (2016) Safety profile of incobotulinum toxin A [Xeomin((R))] in gastrocnemious muscles injections in children with cerebral palsy: Randomized double-blind clinical trial. Eur J Paediatr Neurol 20:532-537.

35. Hasnat MJ and Rice JE. (2015) Intrathecal baclofen for treating spasticity in children with cerebral palsy. [Review]. Cochrane Database of Systematic Reviews 11:CD004552.

36. Spader HS, Bollo RJ, Bowers CA et al. (2016) Risk factors for baclofen pump infection in children: a multivariate analysis. J Neurosurg Pediatr 17:756-762.

37. Carty CP, Walsh HP, Gillett JG et al. (2014) The effect of femoral derotation osteotomy on transverse plane hip and pelvic kinematics in children with cerebral palsy: a systematic review and meta-analysis. [Review]. Gait & Posture 40:333-340.

38. Hesketh K, Leveille L, and Mulpuri K. (2016) The frequency of avn following reconstructive hip surgery in children with cerebral palsy: A systematic review. Journal of Pediatric Orthopaedics.36 (2) (pp e17-e24), 2016.Date of Publication: 2016. e17-e24.

39. Feger MA, Lunsford CD, Sauer LD et al. (2015) Comparative effects of multilevel muscle tendon surgery, osteotomies, and dorsal rhizotomy on functional and gait outcome measures for children with cerebral palsy. PM R 7:485-493.

40. Funk JF, Panthen A, Bakir MS et al. (2015) Predictors for the benefit of selective dorsal rhizotomy. Research in Developmental Disabilities.37 (pp 127-134), 2015.Date of Publication: February 01, 2015. -134.

41. Ailon T, Beauchamp R, Miller S et al. (2015) Long-term outcome after selective dorsal rhizotomy in children with spastic cerebral palsy. Childs Nerv Syst 31:415-423.

42. Tedroff K, Lowing K, and Astrom E. (2015) A prospective cohort study investigating gross motor function, pain, and health-related quality of life 17 years after selective dorsal rhizotomy in cerebral palsy. Developmental Medicine and Child Neurology.57 (5) (pp 484-490), 2015.Date of Publication: 01 May 2015. 484-490.

43. Gillick BT, Krach LE, Feyma T et al. (2014) Primed low-frequency repetitive transcranial magnetic stimulation and constraint-induced movement therapy in pediatric hemiparesis: a randomized controlled trial. Developmental medicine and child neurology 56:44-52.

44. Gillick BT, Krach LE, Feyma T et al. (2015) Safety of primed repetitive transcranial magnetic stimulation and modified constraint-induced movement therapy in a randomized controlled trial in pediatric hemiparesis. Archives of Physical Medicine & Rehabilitation 96:Suppl-13.

45. Kirton A, Andersen J, Herrero M et al. (3-5-2016) Brain stimulation and constraint for perinatal stroke hemiparesis: The PLASTIC CHAMPS Trial. Neurology 86:1659-1667.

46. Collange Grecco LA, de Almeida Carvalho DN, Mendonca ME et al. (2015) Effects of anodal transcranial direct current stimulation combined with virtual reality for improving gait in children with spastic diparetic cerebral palsy: a pilot, randomized, controlled, double-blind, clinical trial. Clinical Rehabilitation 29:1212-1223.

47. Pool D, Valentine J, Bear N et al. (2015) The orthotic and therapeutic effects following daily community applied functional electrical stimulation in children with unilateral spastic cerebral palsy: a randomised controlled trial. BMC Pediatrics 15:154.

48. El-Shamy SM. (2014) Effect of whole-body vibration on muscle strength and balance in diplegic cerebral palsy: a randomized controlled trial. American journal of physical medicine & rehabilitation / Association of Academic Physiatrists 93:114-121.

49. Saquetto M, Carvalho V, Silva C et al. (2015) The effects of whole body vibration on mobility and balance in children with cerebral palsy: A systematic review with meta-analysis. Journal of

Musculoskeletal Neuronal Interactions.15 (2) (pp 137-144), 2015.Date of Publication: 01 Jun 2015. 137-144.

50. El-Shamy SM, Eid MA, and El-Banna MF. (2014) Effect of extracorporeal shock wave therapy on gait pattern in hemiplegic cerebral palsy: a randomized controlled trial. American Journal of Physical Medicine & Rehabilitation 93:1065-1072.

51. Kang M, Min K, Jang J et al. (2015) Involvement of Immune Responses in the Efficacy of Cord Blood Cell Therapy for Cerebral Palsy. Stem Cells and Development.24 (19) (pp 2259-2268), 2015.Date of Publication: 01 Oct 2015. 2259-2268.

52. Legg J, Davies E, Raich AL et al. (2014) Surgical correction of scoliosis in children with spastic quadriplegia: benefits, adverse effects, and patient selection. Evidencebased Spinecare Journal 5:38-51.